MY SYNDROMES' BOOK

By

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اهداء الي روح استاذتي و معلمتي خلقا قبل العلم

الأستاذة الدكتورة دعاء مصطفي توفيق

رئيسة وحدة الكلي

مستشفي الاطفال جامعة الزقازيق

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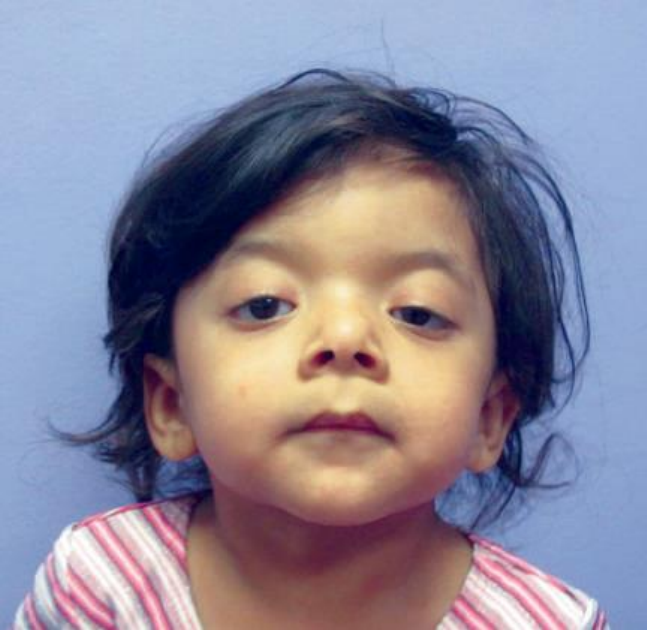
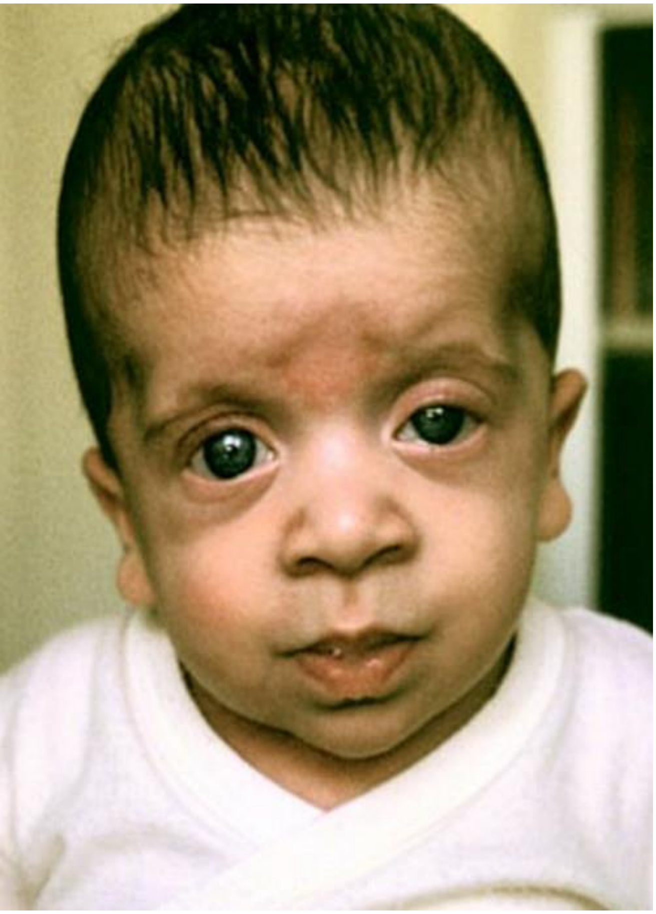
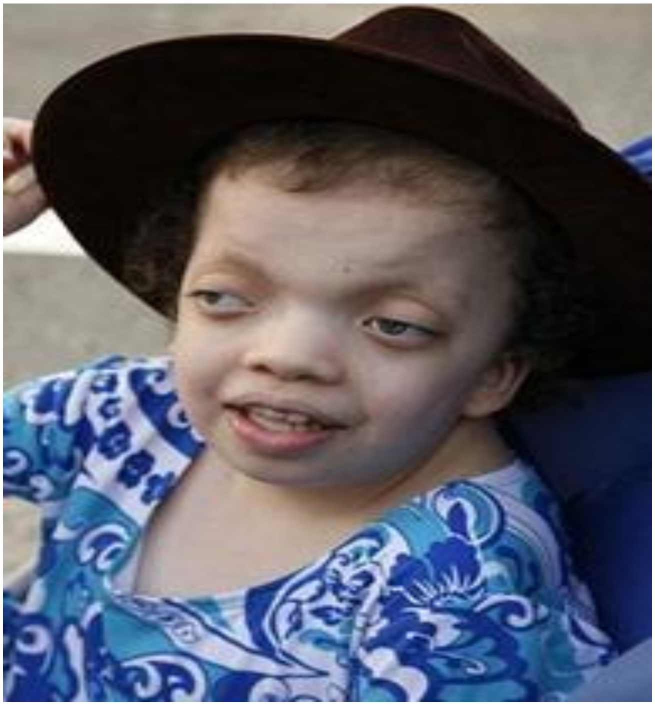
لن انساك ابدا







The acronym NOONANS can be used as an aide-mémoire:

N Neurodevelopmental problems: 25% learning disability, 10–15% special education, <30% mild intellectual impairment, 72% articulation problems, nonverbal abilities better than verbal, specific learning problems/Neuromuscular examination—hypotonia (floppy strong): joint hyperextensibility/ Neurosurgical—Arnold–Chiari type I

O Obstructive heart lesions: RVOT (pulmonary valve); LVOT (HCM)/Other: ASD, VSD, tetralogy of Fallot, coarctation of aorta, branch pulmonary artery stenosis

O Ocular anomalies in up to 95%: strabismus, refractive errors, amblyopia, nystagmus; hypertelorism, epicanthic folds, droopy eyelids, vivid blue or blue– green irises

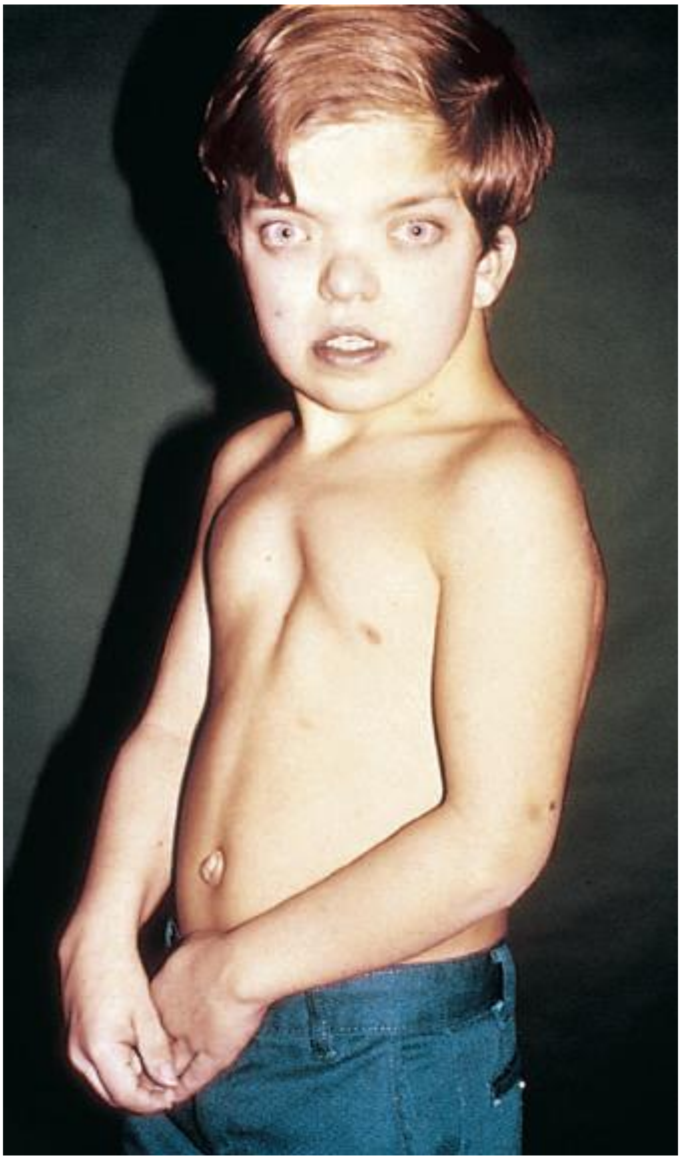
N Neoplasia risk: juvenile myelomonocytic leukaemia (JMML); myeloproliferative disorders; Noonan-like/multiple giant-cell lesion syndrome (granulomas and joint and bone anomalies); hepatosplenomegaly (related to subclinical myelodysplasia)

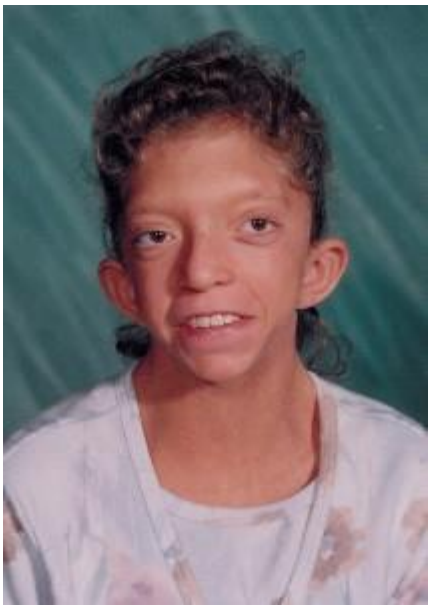
A Abnormal coagulation (33% have one or more defects)/Abnormal lymphatics: lymphoedema (hands/feet/scrotum/vulva), lymphangiectasia (lung, gut or testis)

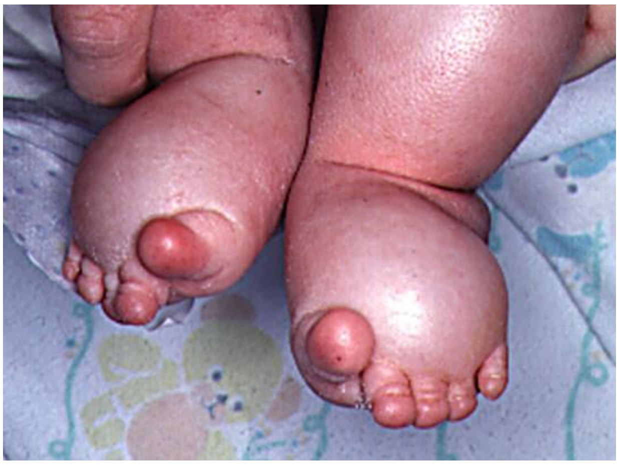
N Neck webbing, with low-set posteriorly rotated ears/Nipples appear low-set/

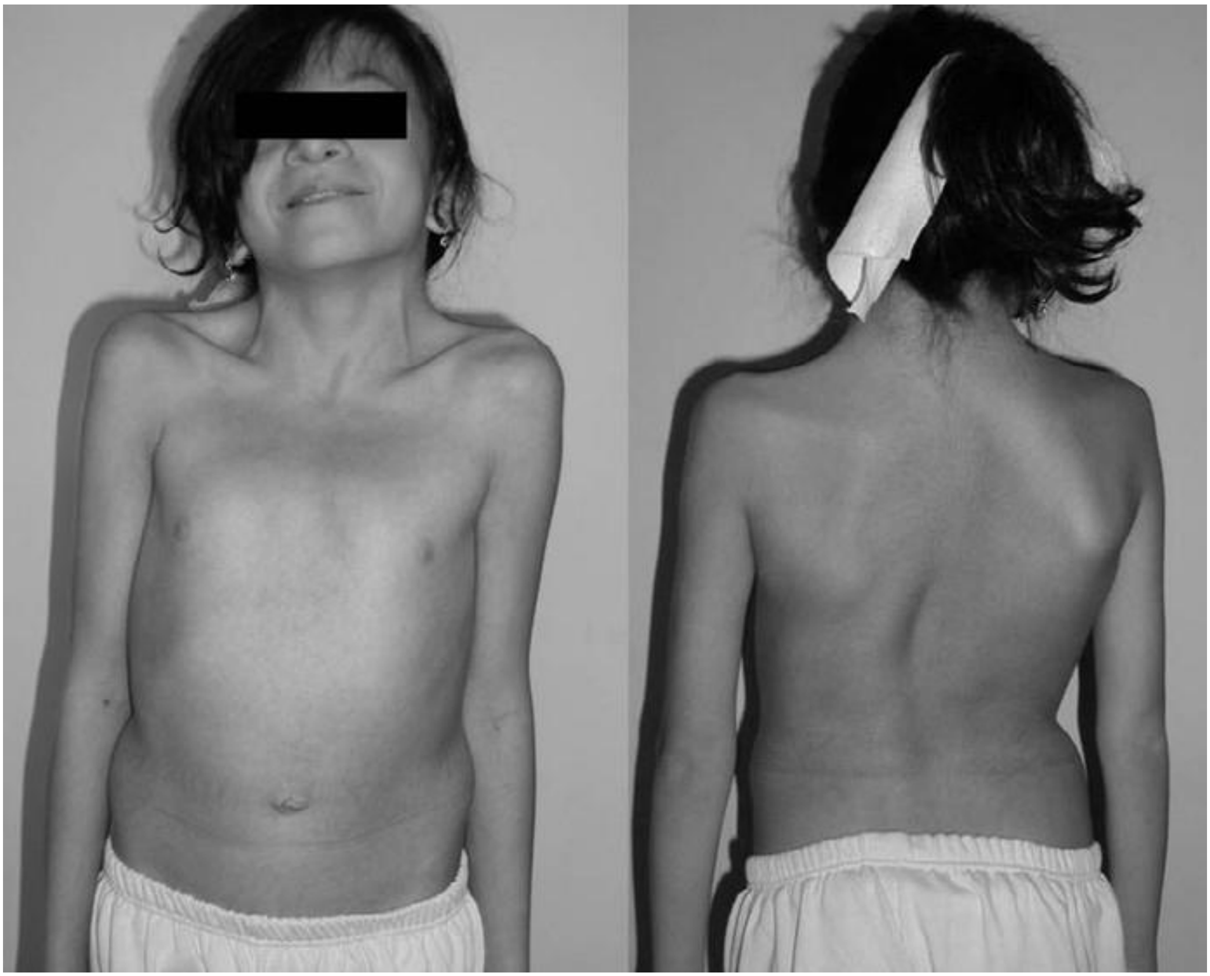
Nephrological anomalies: duplex collecting systems, renal hypoplasia

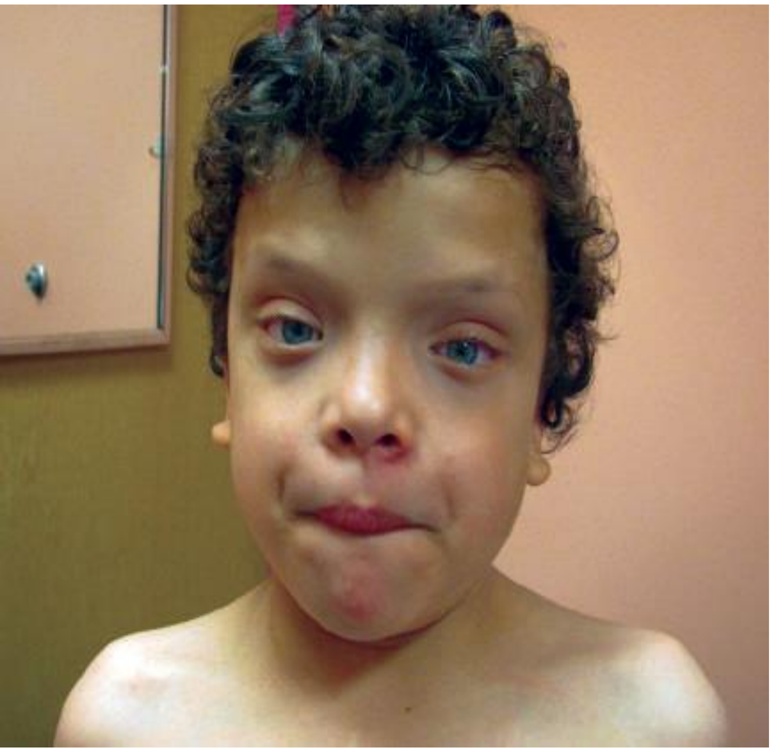
S Sternal deformity (superior carinatum, inferior excavatum)/Short stature (GHRx)/Secondary sexual characteristics: delayed puberty, cryptorchidism in males/ Skin findings: pigmented naevi (25%), café-au-lait patches (10%), lentigines (3%)







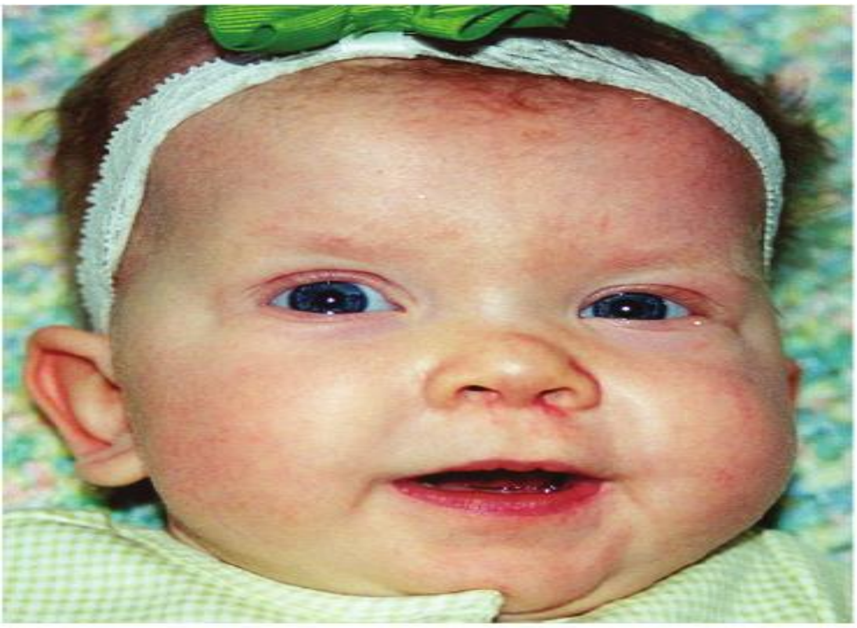


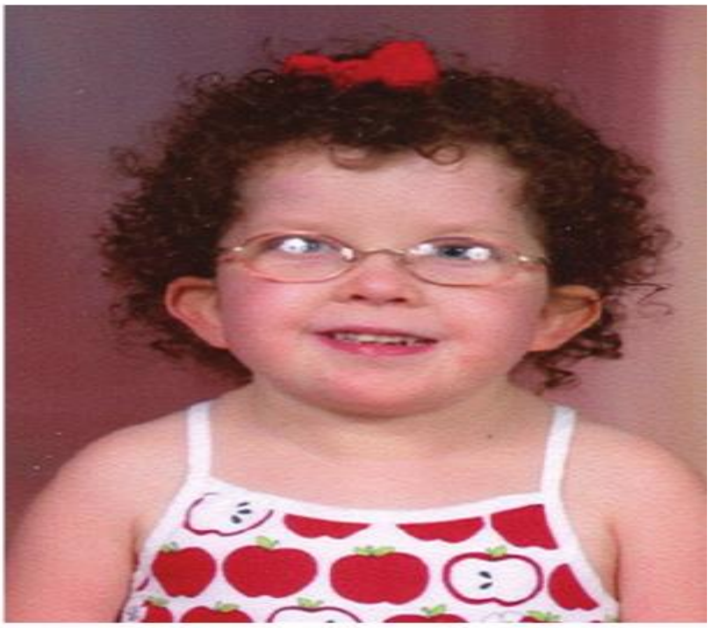


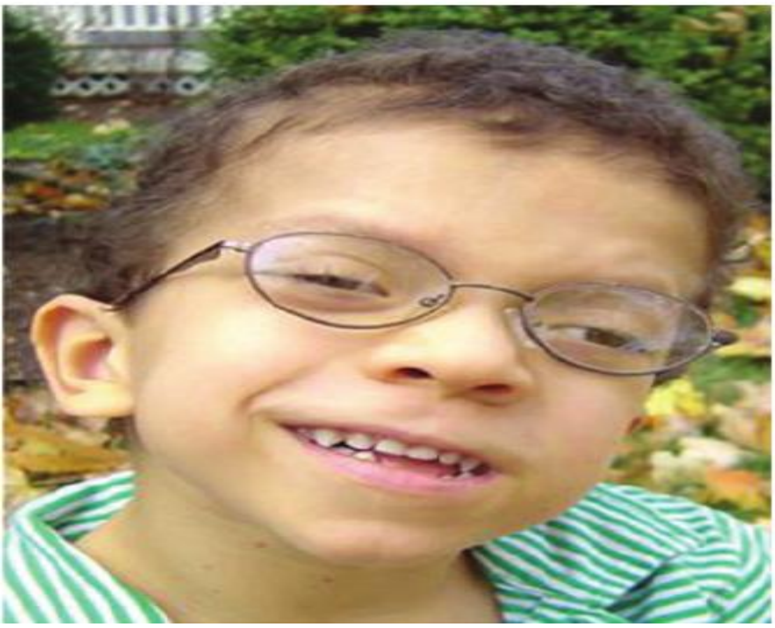
Cardio-fascio-cutanouse

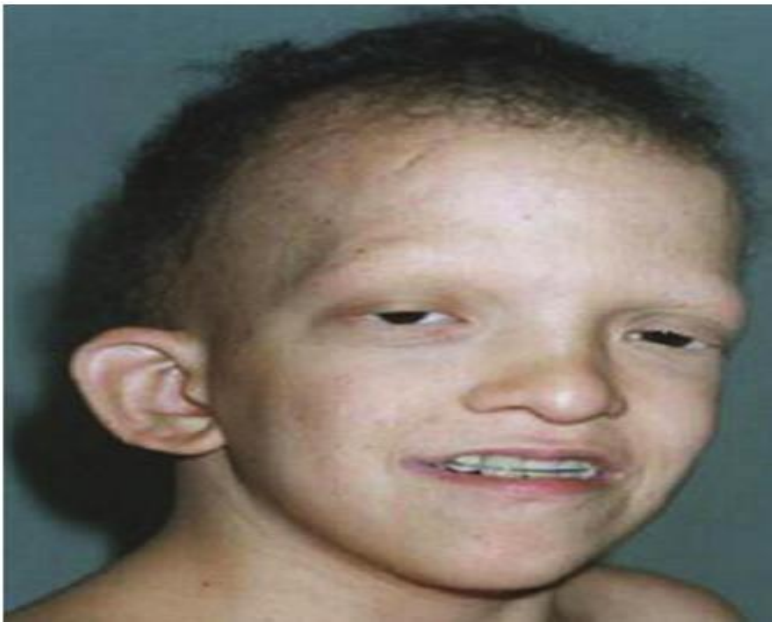
(cardiac lesions—pulmonary valve stenosis; atrial septal defects); hyperkeratosis, haemangiomata, icthyosis. Four genes associated: BRAF (70–80%), MAPK1 and MAPK2 (10–15%), and KRAS (<5%).

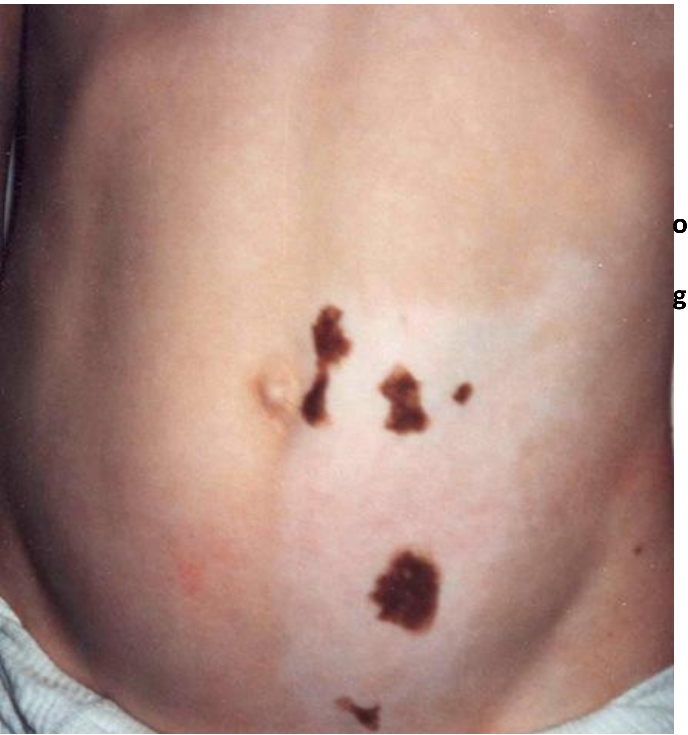
- **Fast growth of nails**
- **Sparse arm and leg hair**
- **Prepubertal axillary odor**
- **Poor hair growth on scalp**
- **Ear lobe creases**
- **Xerosis/eczema**
- **Lymphedema**
- **Generalized hyperpigmentation**





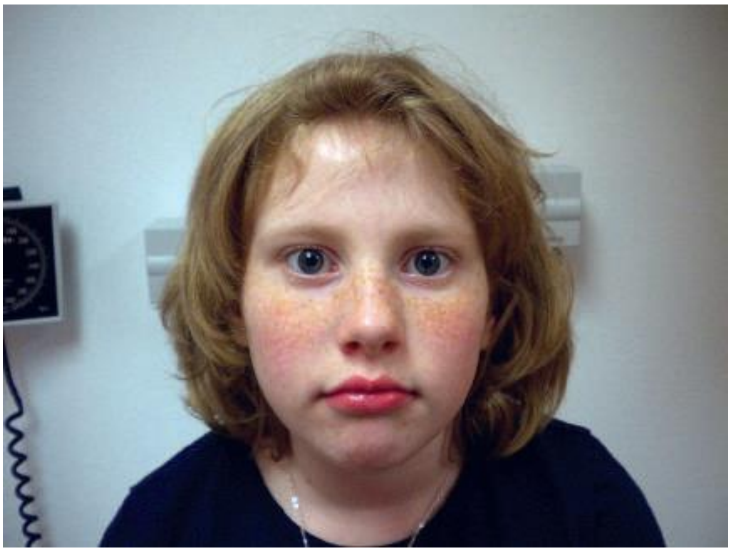


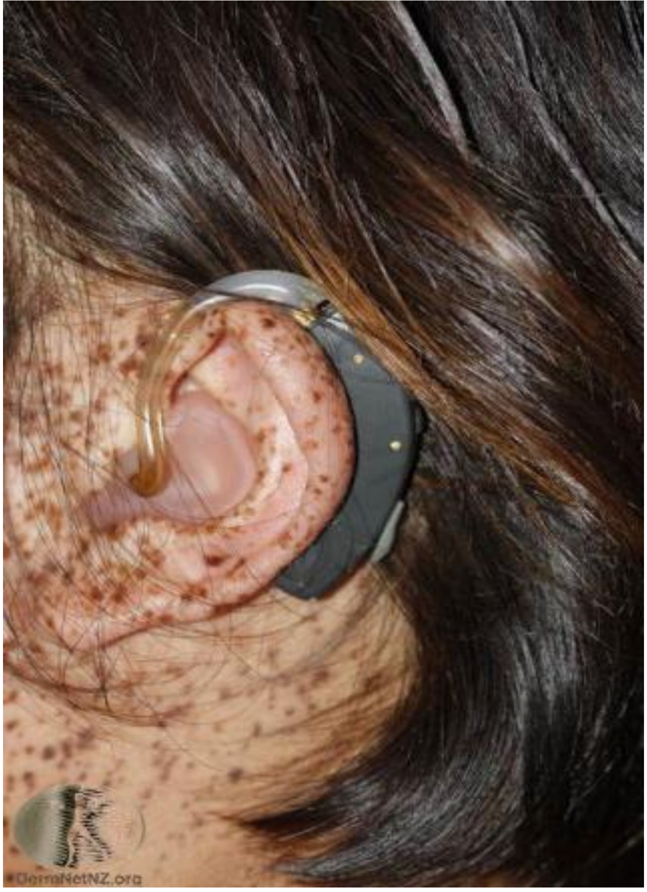


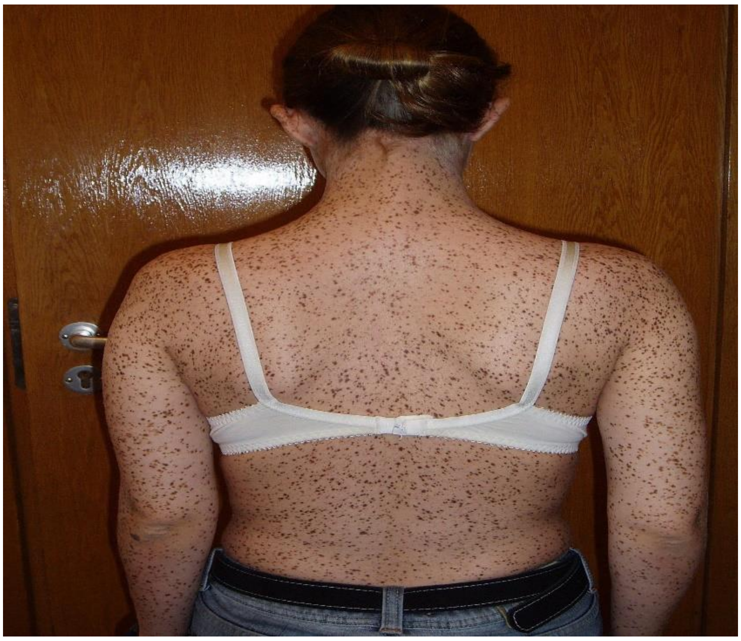


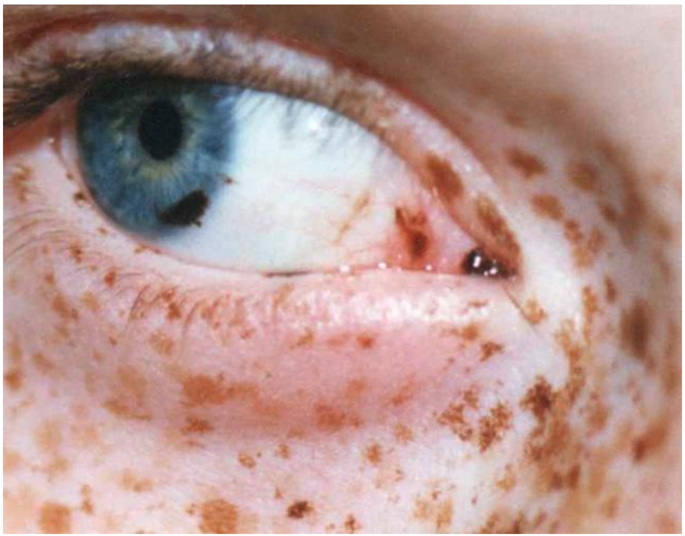
LEOPARD syndrome

(Lentigines, ECG abnormalities [axis deviations, unilateral or bilateral hypertrophy, conduction abnormalities], Ocular hypertelorism, Pulmonary stenosis, Abnormalities of genitalia, Retardation of growth, and Deafness). Two genes associated: PTPN11 and RAF1; testing these finds mutations in 93% of affected people



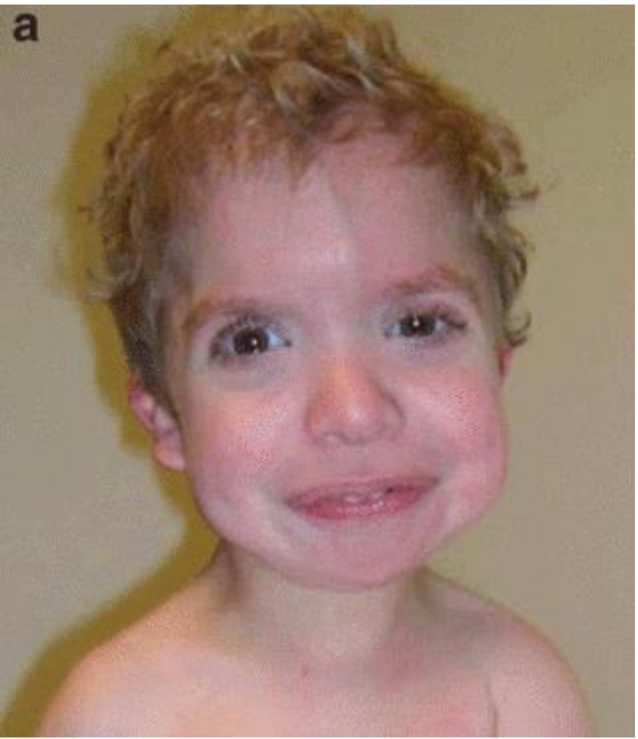


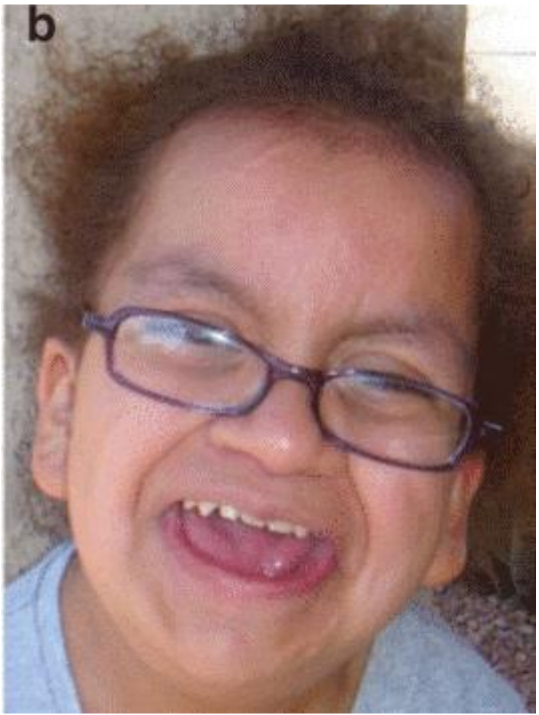


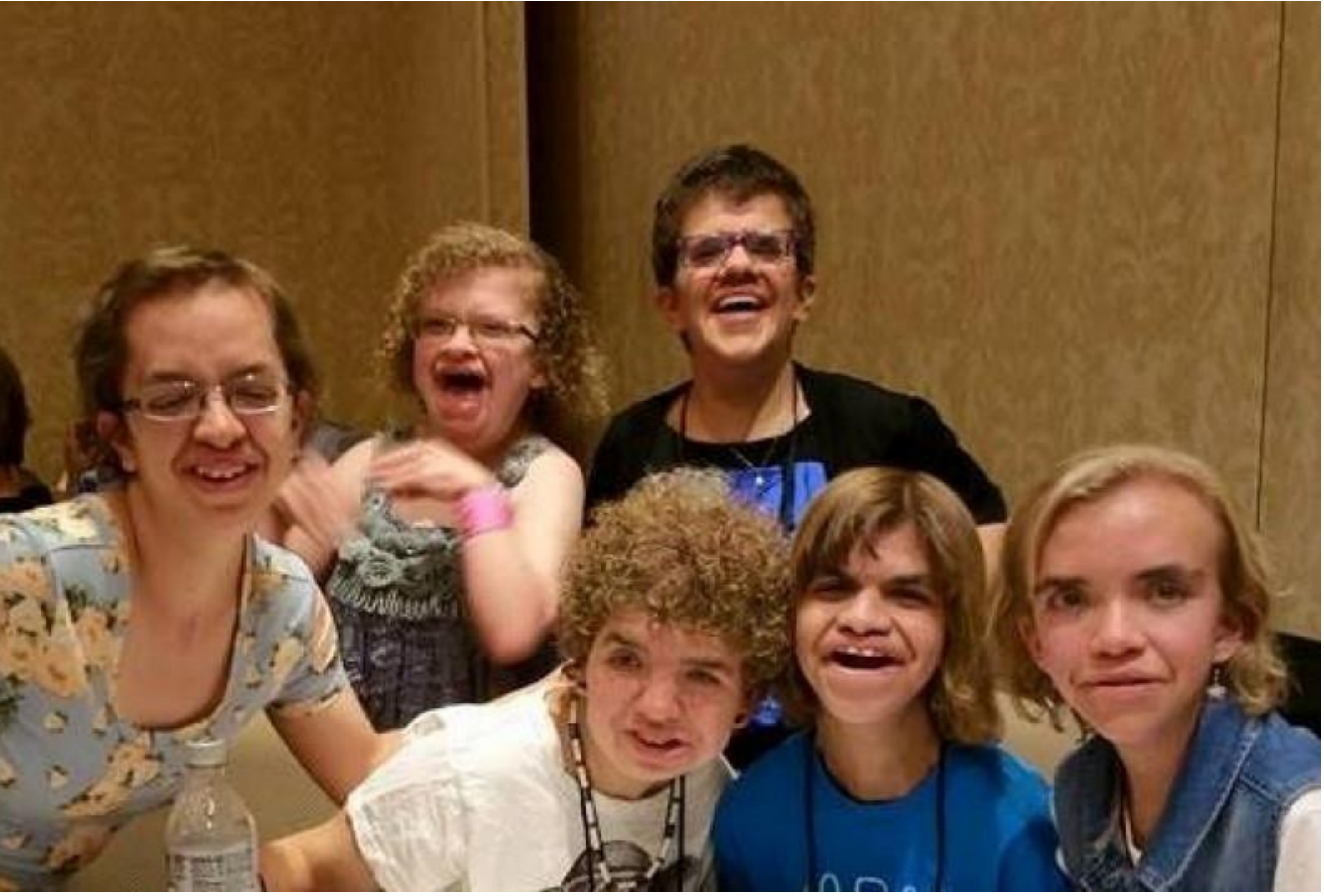


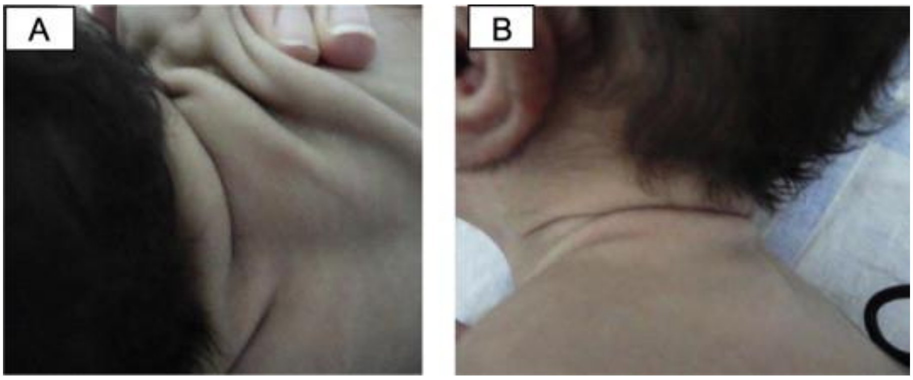
Costello syndrome

gene map locus 11p15.5. Gene: the HRAS proto-oncogene; phenotypic overlap with NS and CFC. Features: short stature, pulmonary stenosis, HCM, hypertelorism, epicanthic folds, intellectual development variable.





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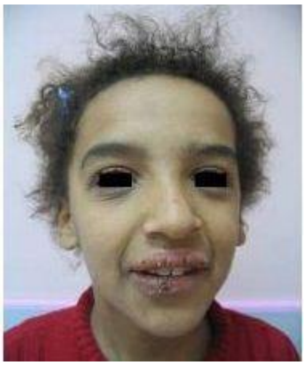

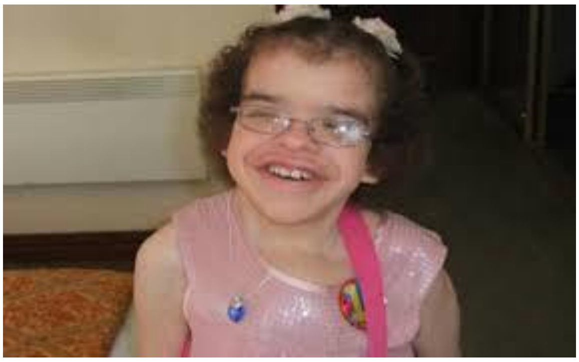

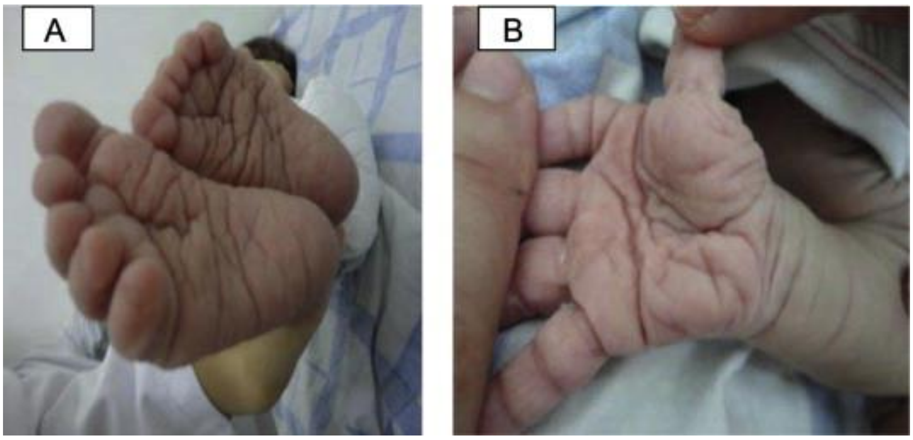
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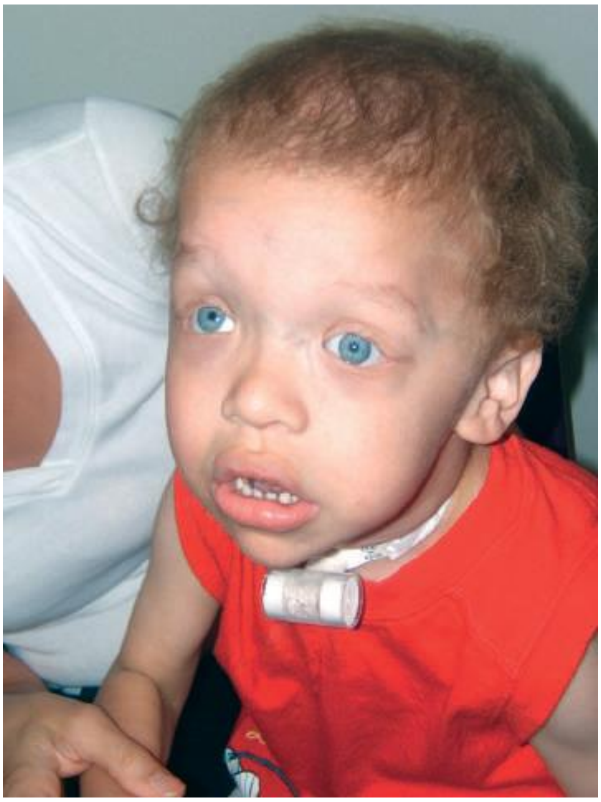


The acronym CATCH-22 can be expanded to CATCHING, to include more features: Digoerge

C Cardiac: 74%; Conotruncal; 3 Ts, 3As, 3Ps (see text above); causes > 90% of all deaths

A Abnormal face: long face, malar flatness, hypertelorism, hooded eyelids, ptosis, ear anomalies (overfolded helices, cupped, microtic, protruberant ears, preauricular pits), prominent nasal root, bulbous nasal tip, nasal dimple, asymmetric crying face)/Autoimmune diseases: juvenile idiopathic arthritis, Graves' disease, vitiligo

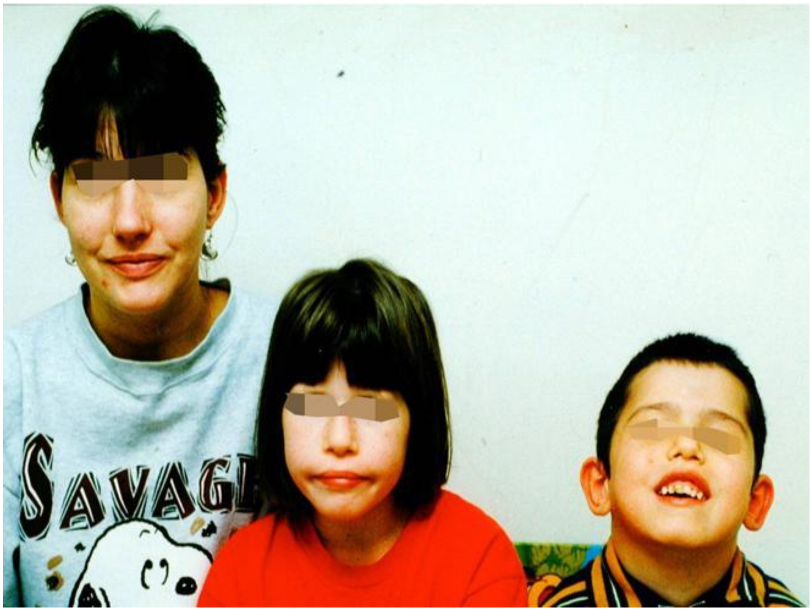
T Thymic hypoplasia, T-cell deficiency; 77% have immunodeficiency

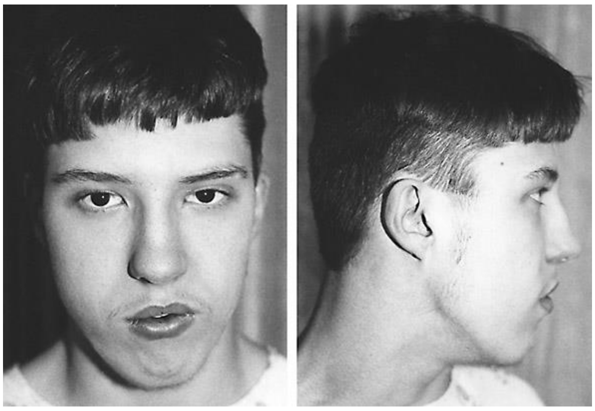
C Cleft palate, and other palatal anomalies: velopharyngeal incompetence (VPI), submucosal cleft palate (SMCP), bifid uvula, cleft lip; 69% have palatal problem/ Craniosynostosis and other skeletal anomalies: hemivertebrae, polydactyly, extra ribs/Croup-like: laryngotrachealoesophageal anomalies—vascular ring, laryngeal web

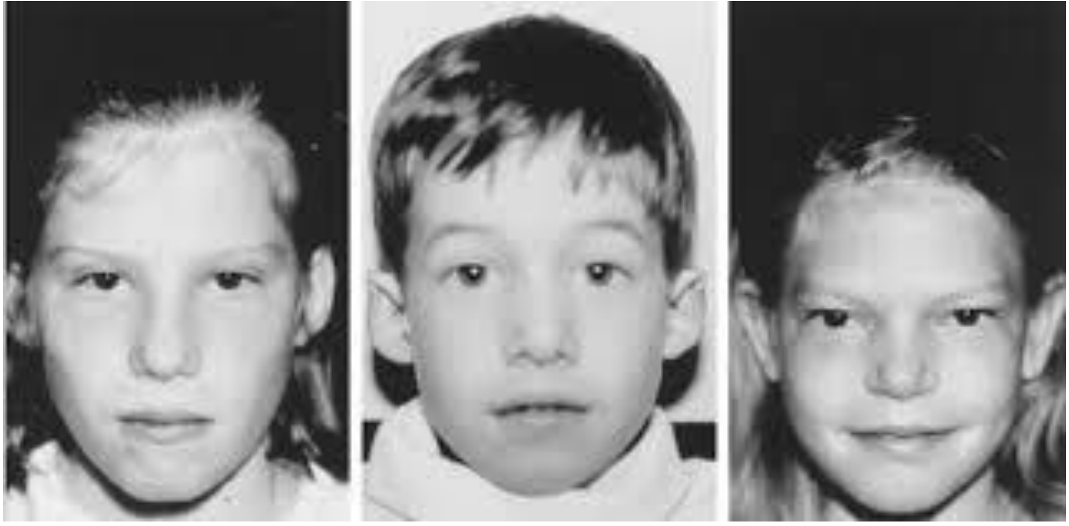
H Hypoparathyroidism/Hypocalcaemia/Hearing loss (conductive and sensorineural)

I Intellectual issues: learning problems (non-verbal), 70–90%; mean full scale IQ 75–80; neuropsychological—ADHD, ASD; schizophrenia, bipolar, anxiety, depression/Impaired swallowing (dysmotile pharyngoesophageal area [derived from 3rd and 4th pharyngeal pouches]; nasopharygeal reflux, abnormal cricopharyngeal closure)

N Neurological: unprovoked fits, neural tube defects, cerebellar atrophy, tethered cord/**Nephrologica**l: dysplastic kidneys, horseshoe kidney, duplicated kidney (37% in all)/**Neoplasia**: hepatoblastoma, neuroblastoma, Wilms, renal cell carcinoma G Growth hormone deficiency/Genitals: hypospadias, cryptorchidism, absent uterus/Gastrointestinal: atresias (oesophageal, jejunal, anal), malrotation, Hirschsprung/GP1BB mutation can cause coexistent Bernard–Soulier syndrome (BSS) (thrombocytopaenia and giant platelets); risk of bleeding significant

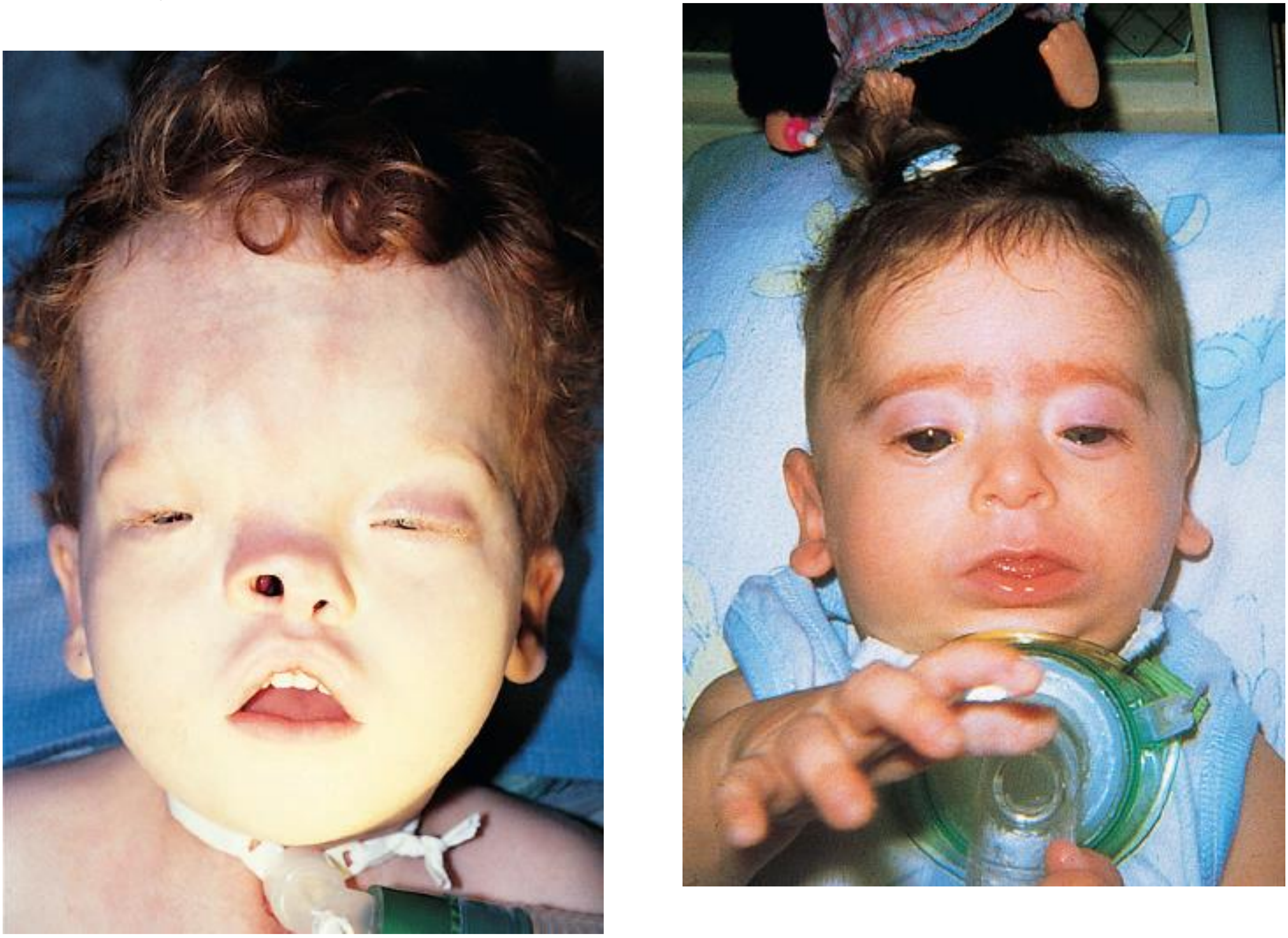






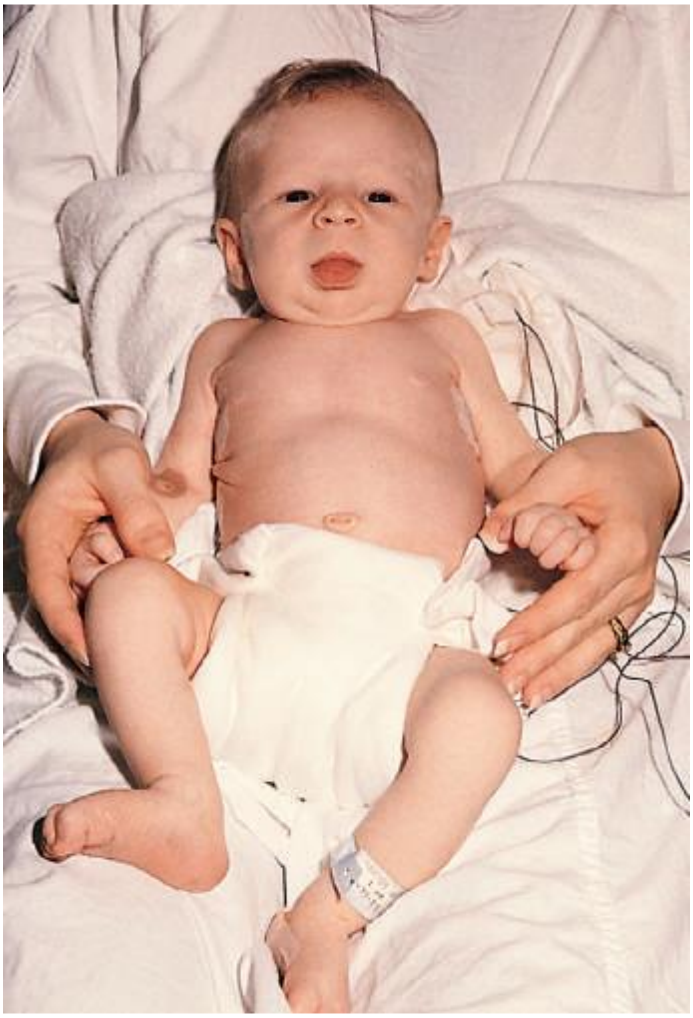
CHARGE association

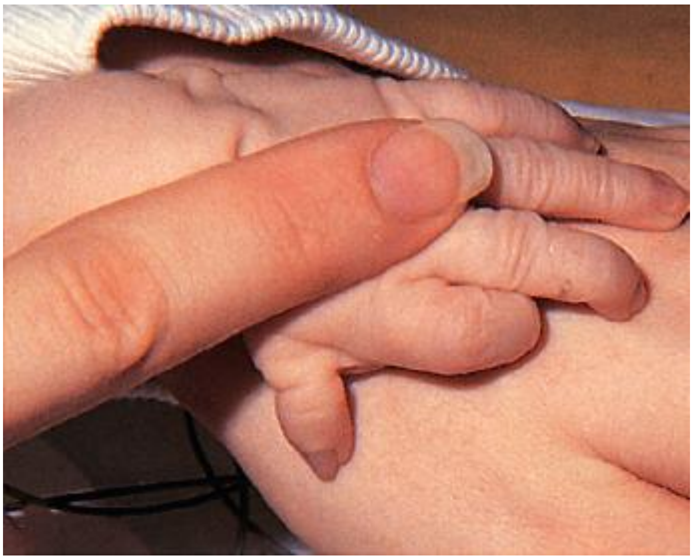
. A, Note the short palpebral fissures and ptosis; low-set, dysplastic ears; and small chin. Choanal atresia necessitated tracheotomy. B, Another example of an infant with CHARGE association has clinical features that include a prominent forehead, hypertelorism, narrow palpebral fissures, hypoplasia of the right naris, low-set ears, and a cupid's-bow mouth. *(A, Courtesy W. Tunnessen, MD.*B, *Courtesy Timothy McBride, MD, Fairfax, VA.)*



This child with VATER association

(A) has facial features that are not dysmorphic, but he has preaxial polydactyly of the thumb (B), which was associated with radial dysplasia.





Williams–Beuren Syndrome

The mnemonic WILLIAMS HYPERCALCAEMIA has most of the salient features of WS:
W Williams–Beuren Syndrome Critical Region (WBSCR); chromosome locus 7q11.2
I Intelligence quotient (IQ) average 50–60/Impaired vision: reduced stereopsis

L Low tone (hypotonia)/Low pitched or hoarse voice, vocal cord paralysis L Lax joints (joint hypermobility)/Loquacious, over-friendly, excessively empathic

I Impaired feeding; tactile sensory defensiveness (difficulty with food textures); vomiting

A ADHD symptomatology/Anxiety (somatisation can lead to abdominal pain)

M Mitral valve prolapse (MVP)

S Supravalvular aortic stenosis (SVAS)/Spine: scoliosis, kyphosis/Sternum: excavatum

HY HYpercalcaemia, hypercalciuria, hypertension

P Peripheral pulmonary arterial stenosis (PPW)/Puberty early (but not precocious)

E Elastin arteriopathy (SVAS, PPS, aortic insufficiency, stenosis of mesenteric arteries)/Endocrine: hypothyroidism; IDDM in adults/Elfin face (see details below under A for appearance)

R Renal anomalies (nephrocalcinosis, pelvic kidney)

C Chronic otitis media (50%)/Characteristic personality: over-friendly, peopleorientated

A Audiological problems: high-frequency sensorineural hearing loss, hyperacusis (in 90%)

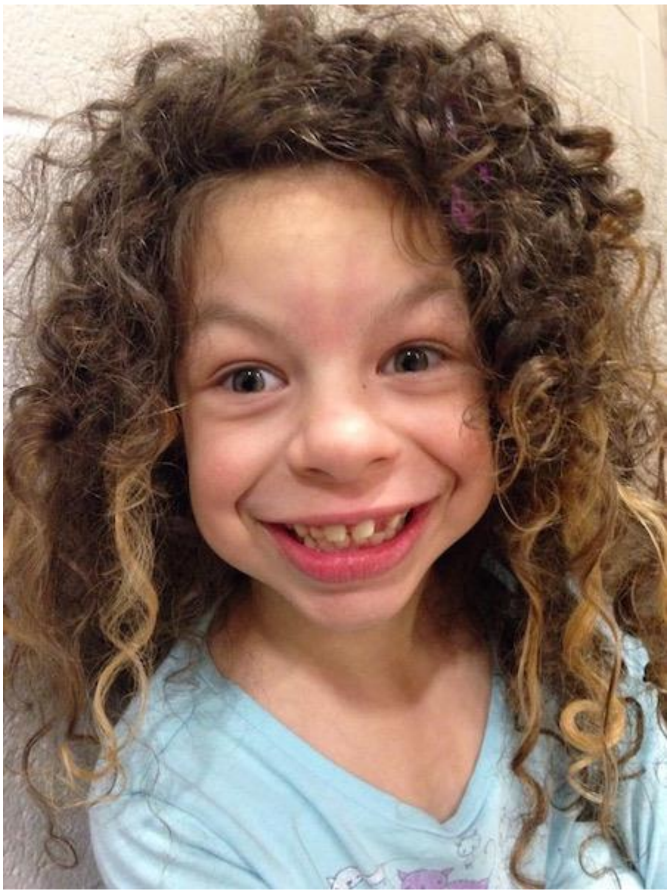
L Linear growth failure; postnatal growth rate 75% of normal/Loquacious personality

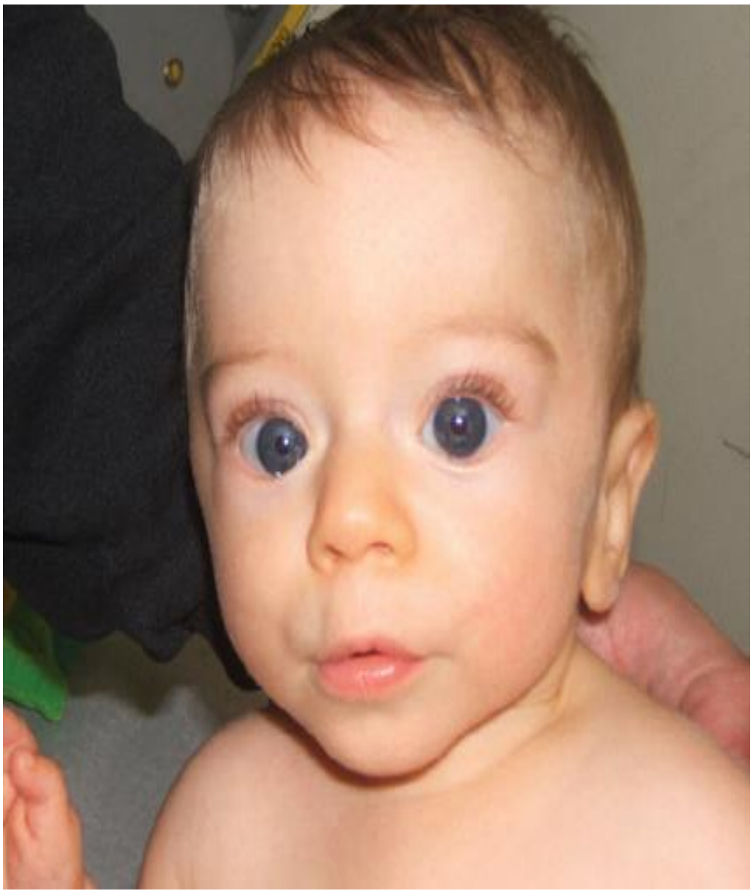
C Cognitive: good verbal short-term memory, language; poor visuospatial construction
A Appearance: broad brow, bitemporal narrowness, medial eyebrow flare, short palpebral fissures, epicanthic folds, blue stellate iris, short nose, full nasal tip, full cheeks, malar hypoplasia, long philtrum, full lips, wide mouth, small jaw, prominent earlobes

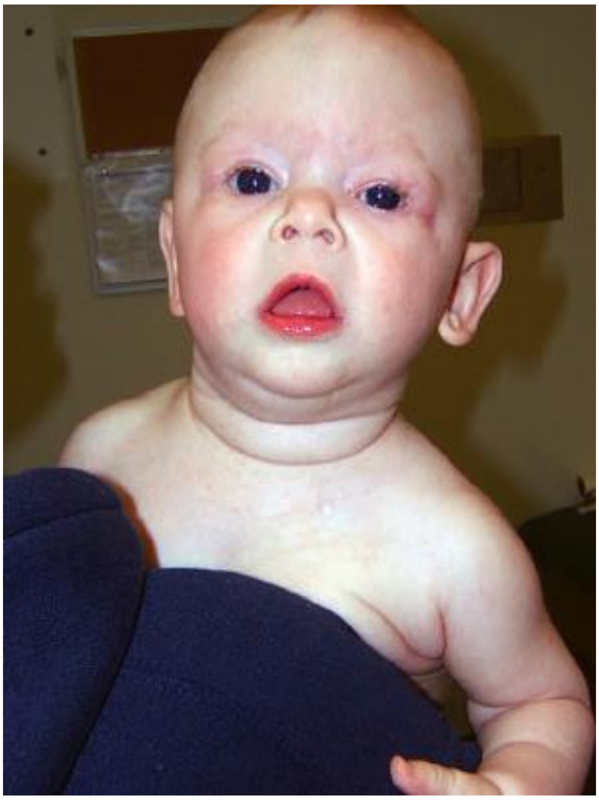
E Eyes: hypotelorism, strabismus (50%), amblyopia, refractive errors (hyperopia in 50%)

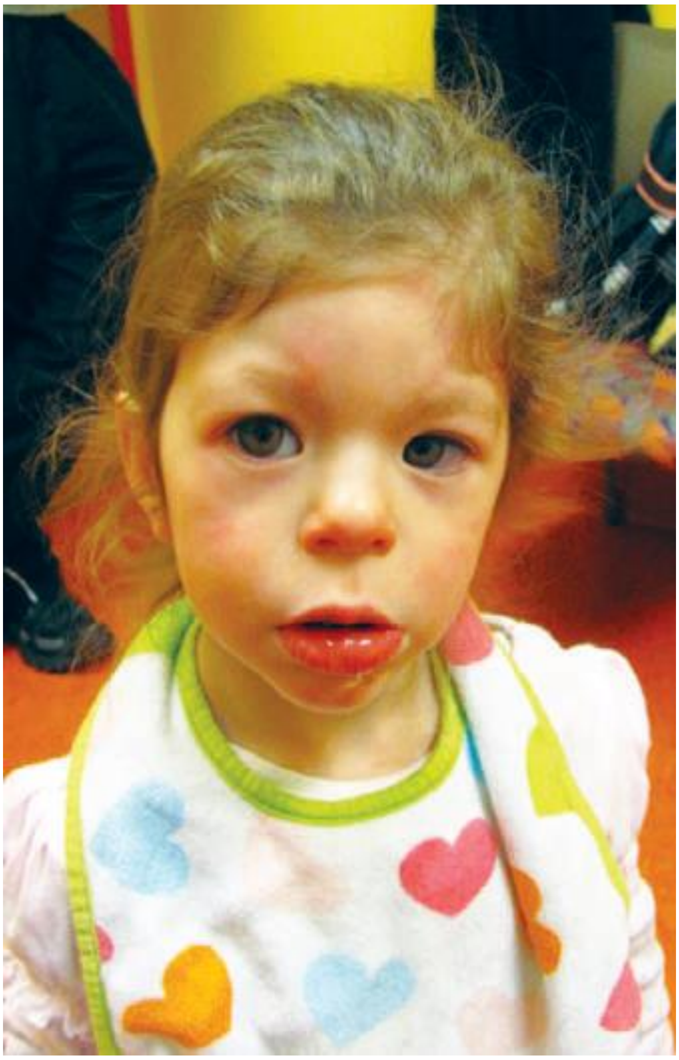
M Malocclusion, microdontia, enamel hypoplasia, widely spaced teeth, missing teeth

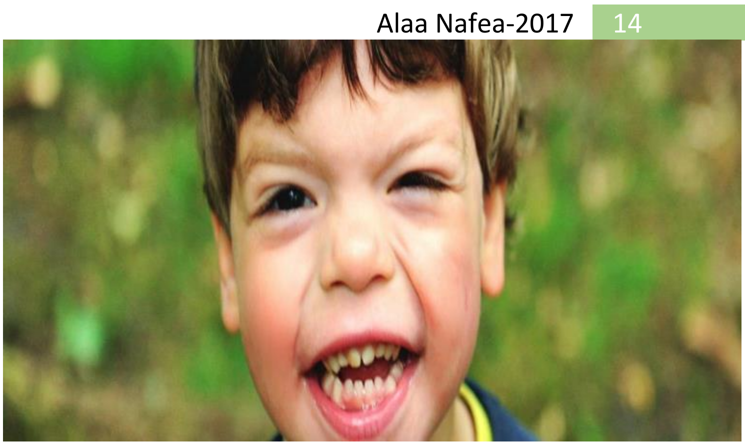
I Intestinal problems: constipation, diverticulosis, coeliac disease
A Abdominal pain: reflux oesophagitis; cholelithiasis; diverticulitis; ischaemic bowel disease

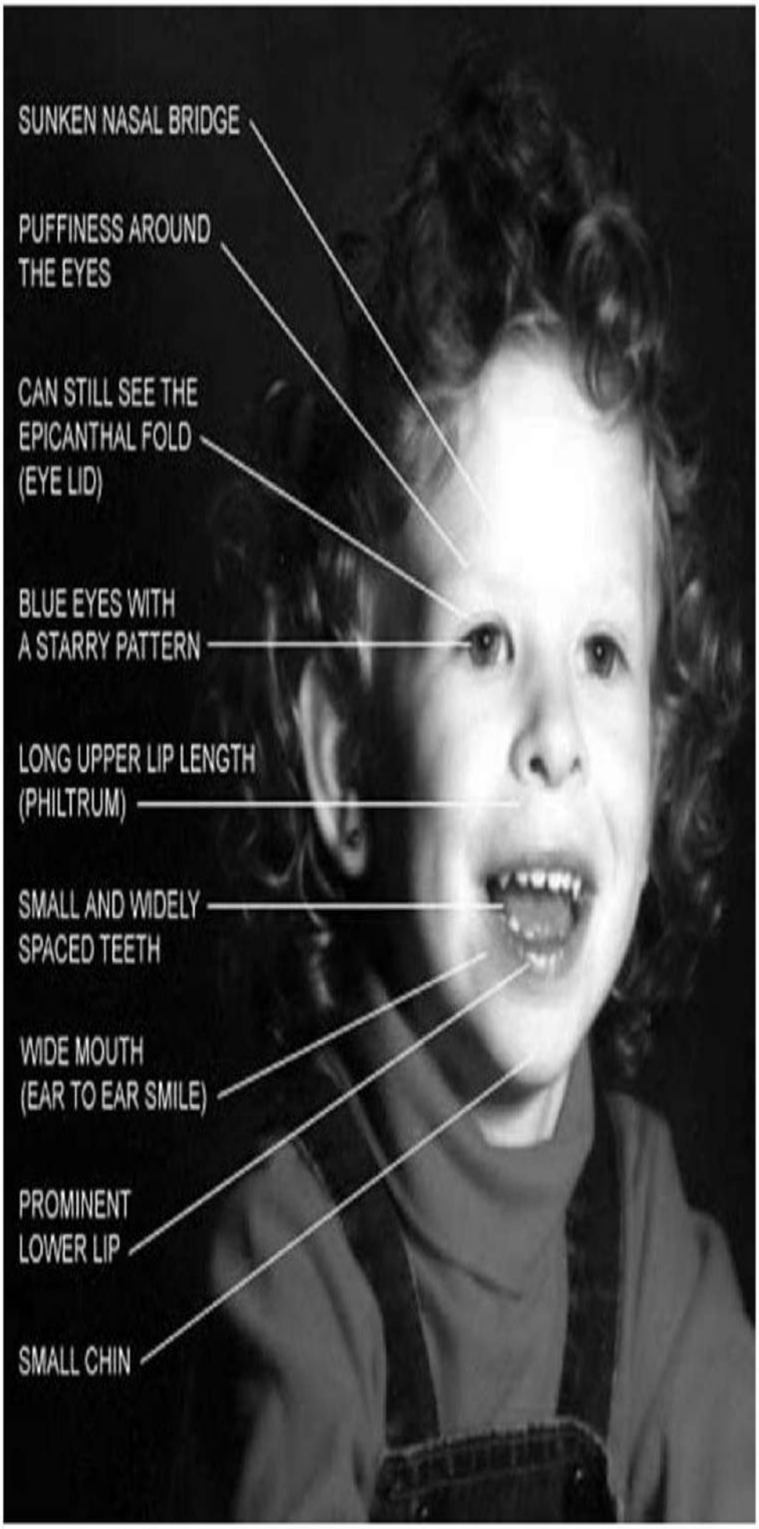


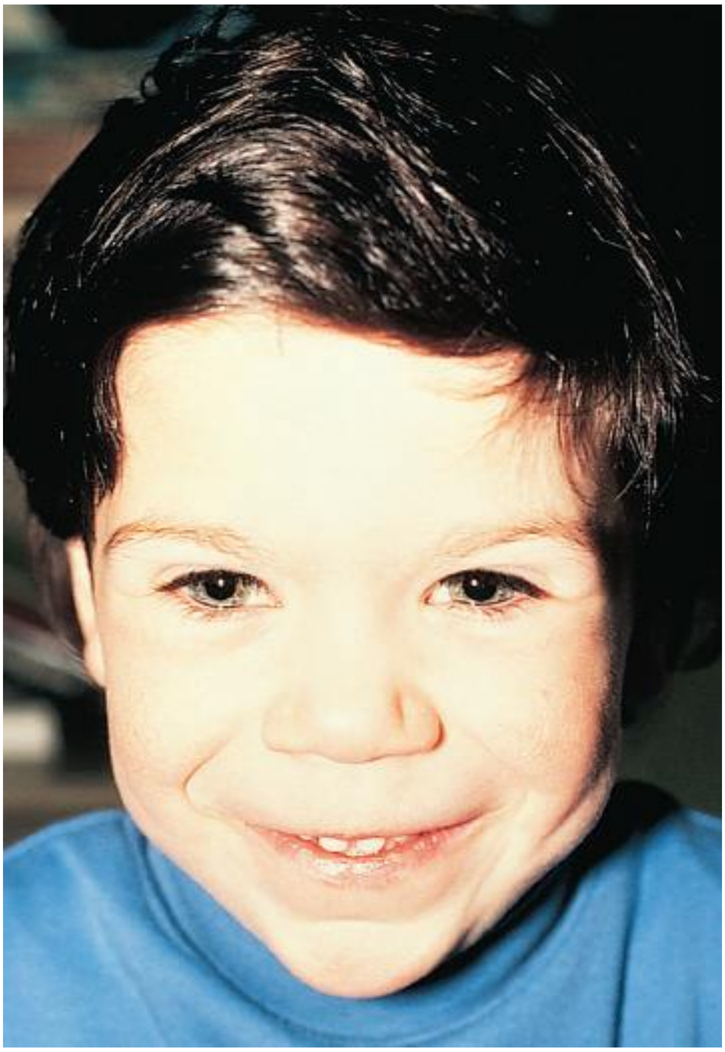








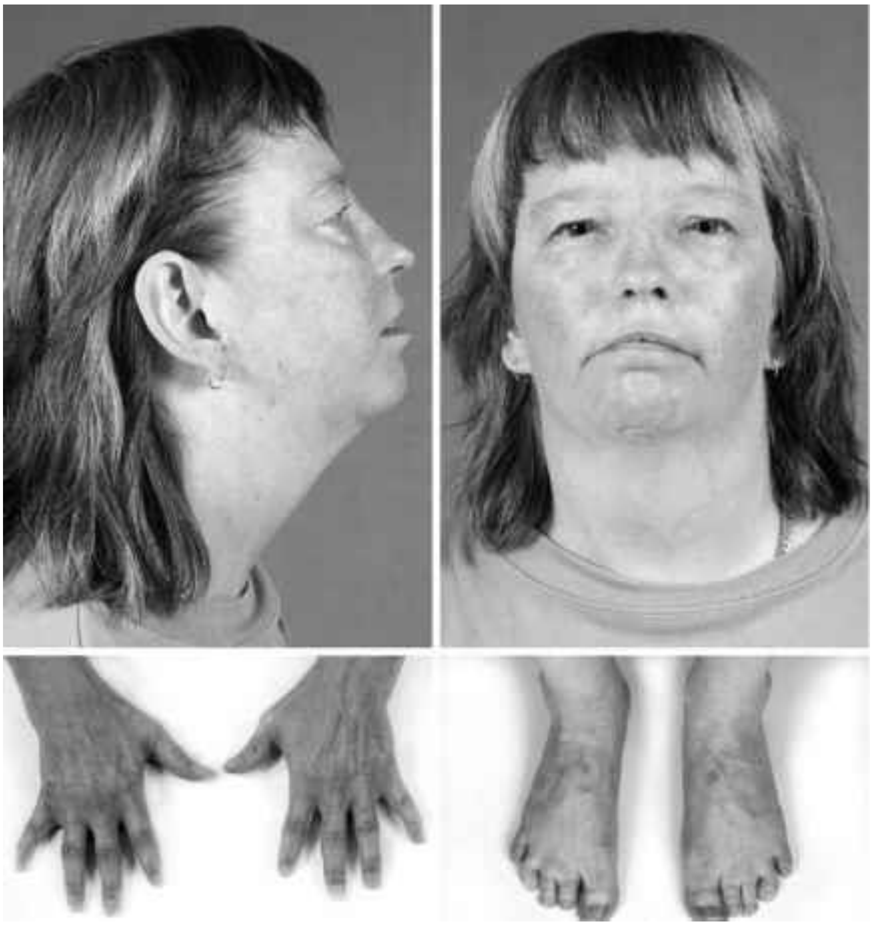

SUNKEN NASAL BRIDGE
PUFFINESS AROUND THE EYES
CAN STILL SEE THE EPICANTHAL FOLD (EYE LID)
BLUE EYES WITH A STARRY PATTERN
LONG UPPER LIP LENGTH (PHILTRUM)
SMALL AND WIDELY SPACED TEETH
WIDE MOUTH (EAR TO EAR SMILE)
PROMINENT LOWER LIP
SMALL CHIN

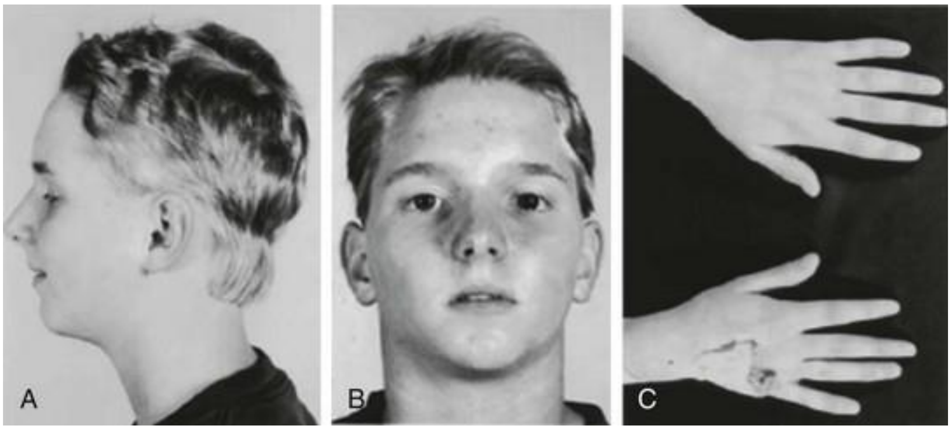


Andersen–Tawil syndrome

(LQTS, episodic flaccid muscle paralysis, and dysmorphic features; potassium channel gene KCNJ2) and Timothy syndrome (LQTS with syndactyly, dysmorphic facial features and neurological disorders; average age of death from VT 2.5 years; calcium channel gene CACA1C; the recommended treatment is ICD)

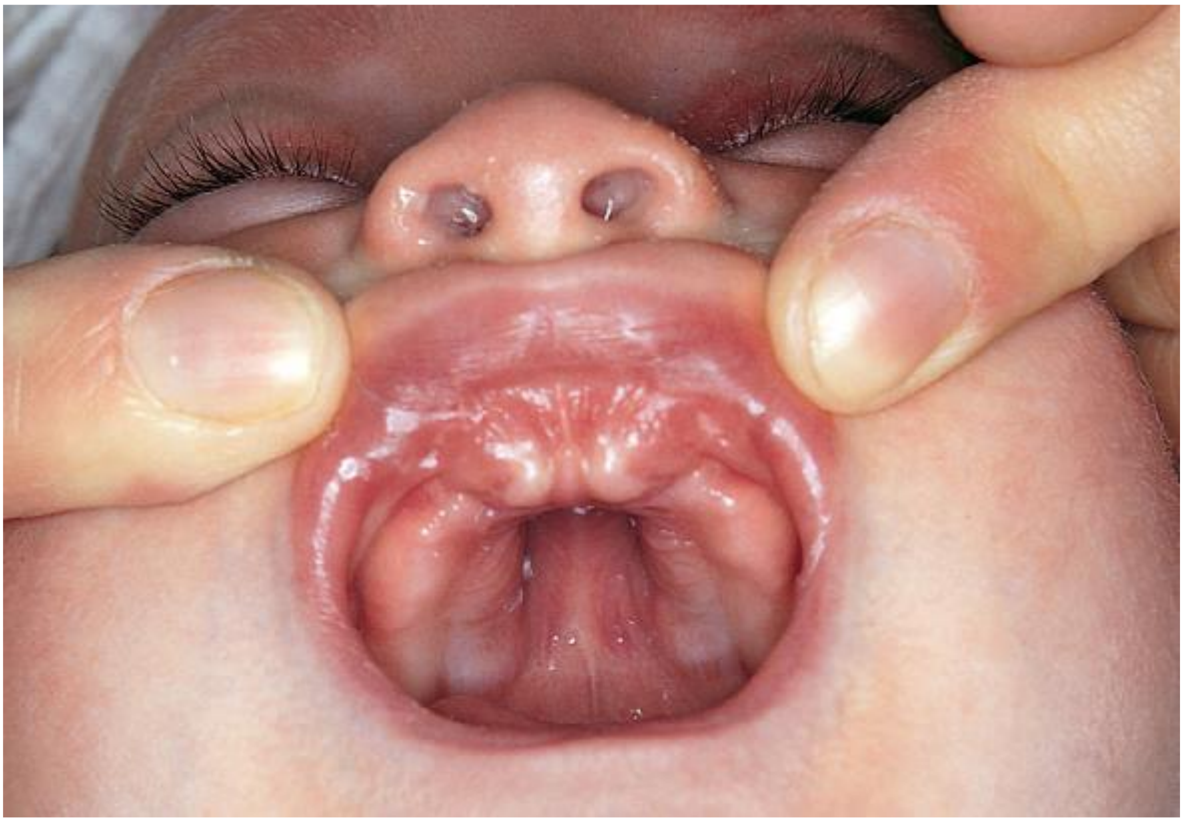
These features often include a very small lower jaw (micrognathia), dental abnormalities, low-set ears, widely spaced eyes, and unusual curving of the fingers or toes (clinodactyly). Some affected people also have short stature and an abnormal curvature of the spine (scoliosis).

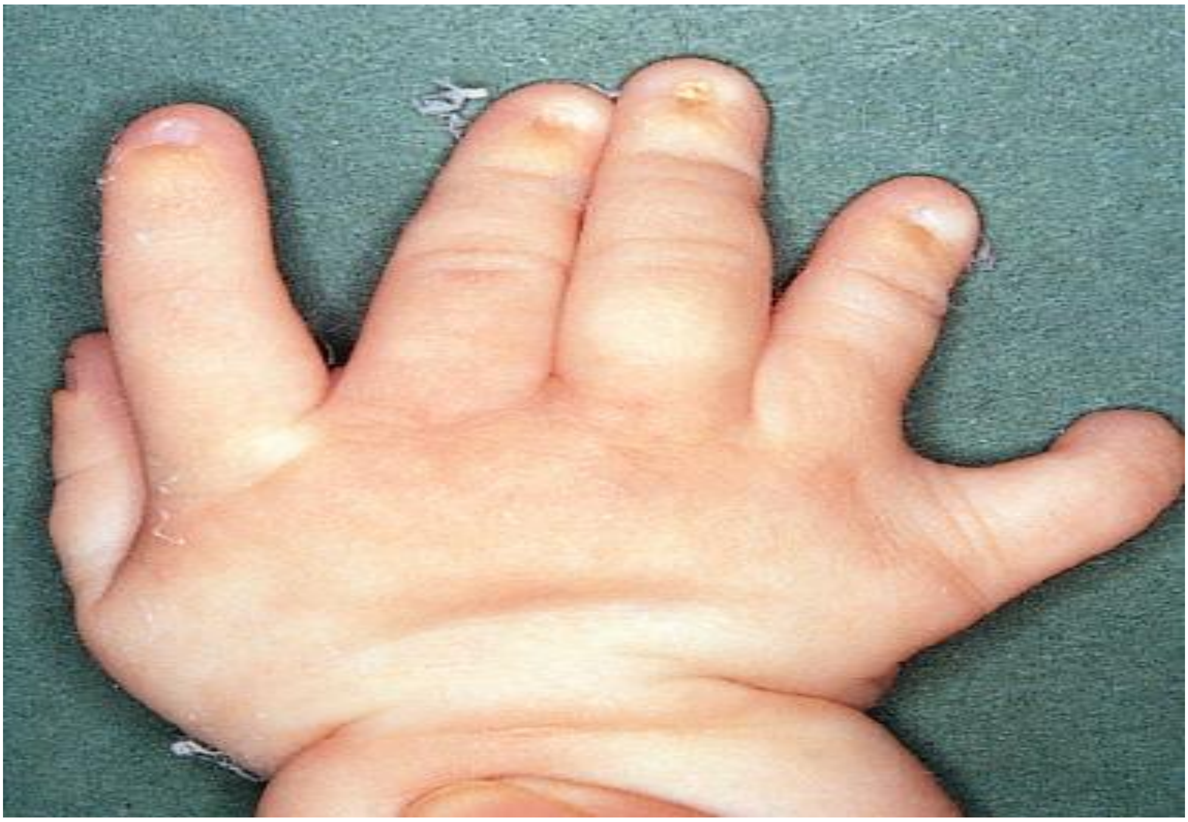




Ellis-van Creveld syndrome

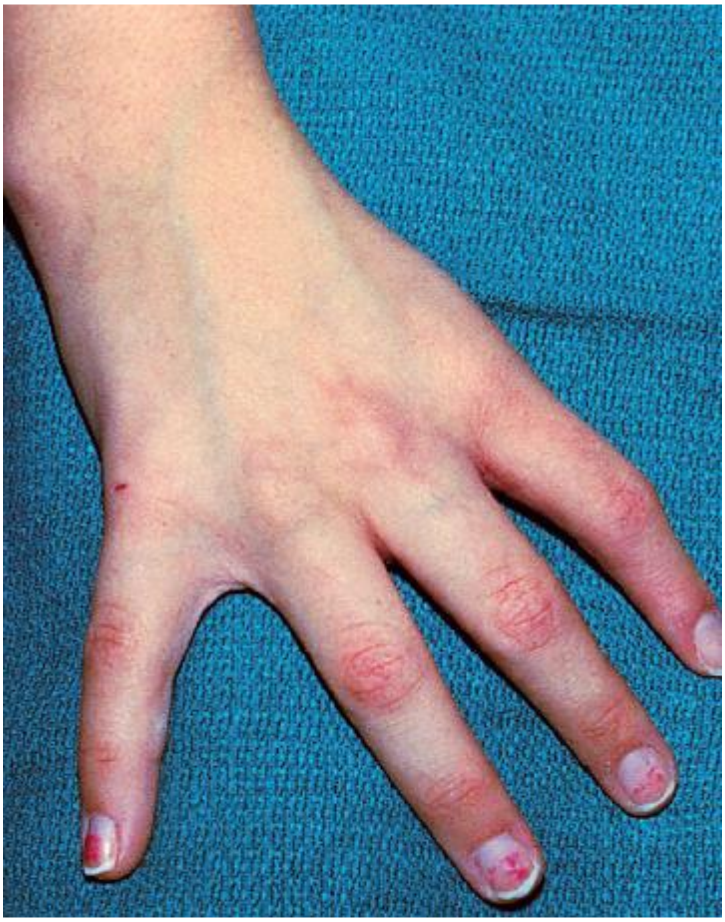
is an autosomal recessive disorder characterized by multiple gingival frenula, natal teeth, and polydactyly. The patient with this syndrome frequently has an atrial septal defect or a common atrium.

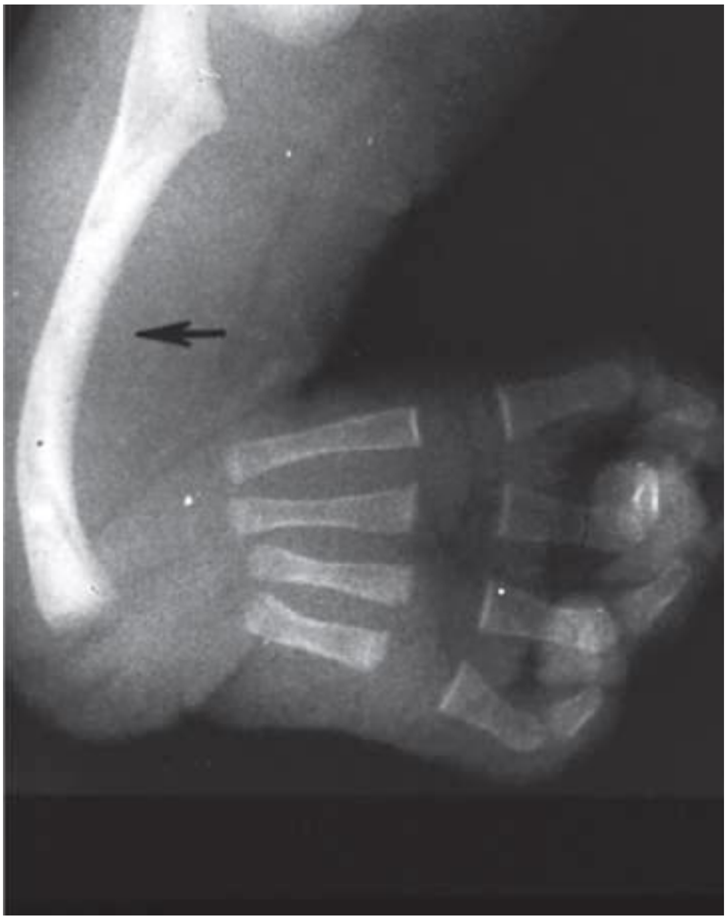




Holt-Oram syndrome

an autosomal dominant disorder, is associated with upper limb deformities consisting of narrow shoulders, hypoplasia of the radius, and phocomelia .Absence of both radius and thumb or proximal displacement of the thumb is the most frequent finding. Commonly associated cardiovascular abnormalities include an atrial septal defect, ventricular septal defect, and arrhythmias (atrial and ventricular ectopy and atrioventricular block).





Marfan Syndrome

The acronym MARFANS also can be used as an (alternative) aide-mémoire:

M Mitral prolapse ± Mitral regurgitation

A Ascending aorta dilatation (involving sinuses of Valsalva)/dissection/Arched palate (high arched, with tooth crowding)/Acetabuli (protrusio acetabuli)

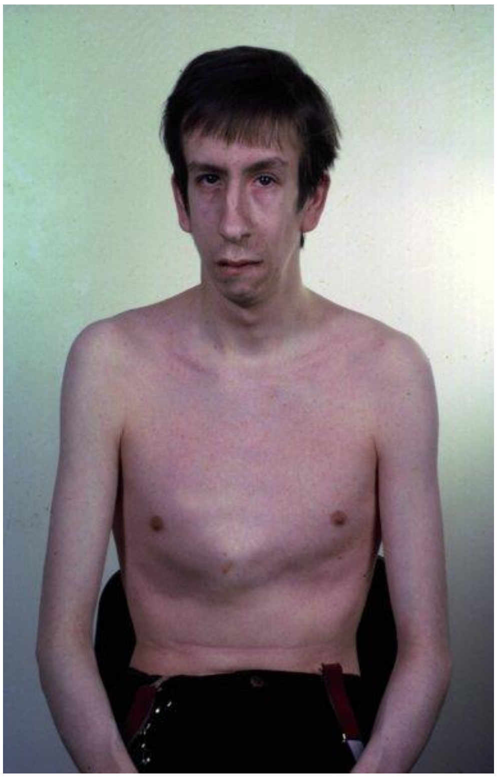
R Regurgitation of aorta/mitral/Retinal detachment/Reduced US:LS ratio

F Fibrillin defective/Facial gestalt (dolichocephaly, down-slanting palpebral fissures, deeply set eyes (enophthalmos), decreased malar prominence (malar hypoplasia), diminished jaw (retrognathia)/Flat cheek bones/Flat cornea/Flexible joints (joint hypermobility)

A Apical blebs (on CXR)/Air leaks (spontaneous pneumothorax)/Arachnodactyly

N Near-sightedness (myopia)/Neurological involvement related to dural ectasia—stretching of dural sac in the lumbosacral region/Nerve entrapment—CSF leak from dural sac (causing postural hypotension and headache)

S Scoliosis/Sternal deformity/Skeletal dolichostenomelia/Sacral dural ectasia.



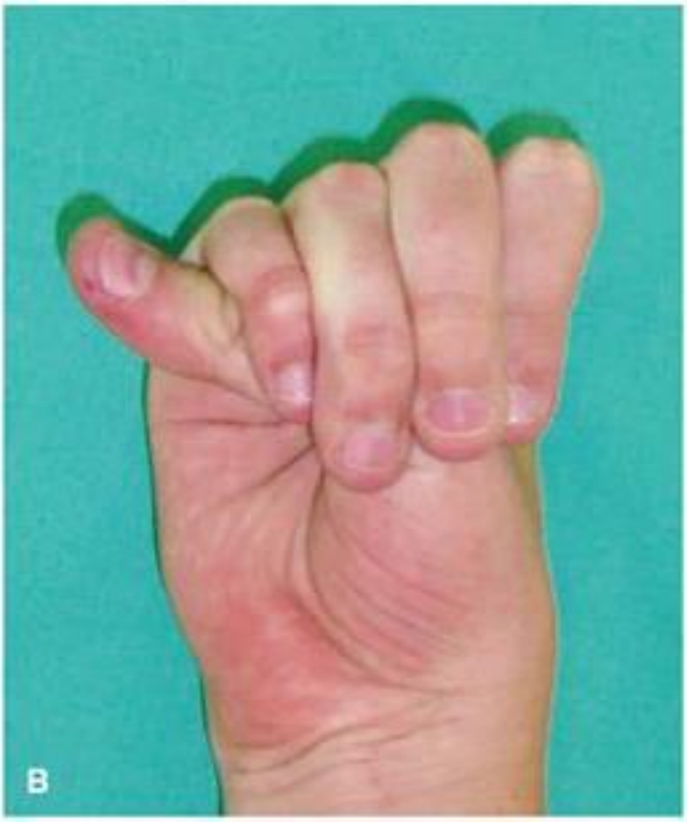
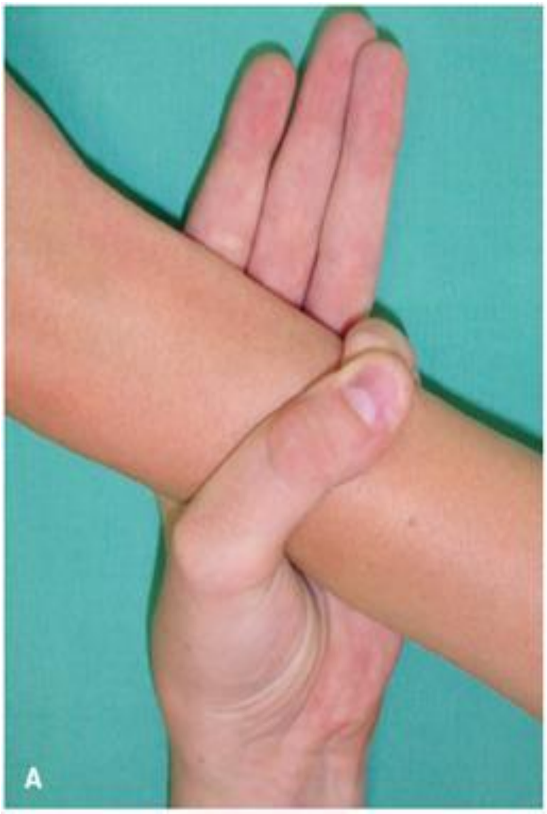


Figure 1steinberg thumb sign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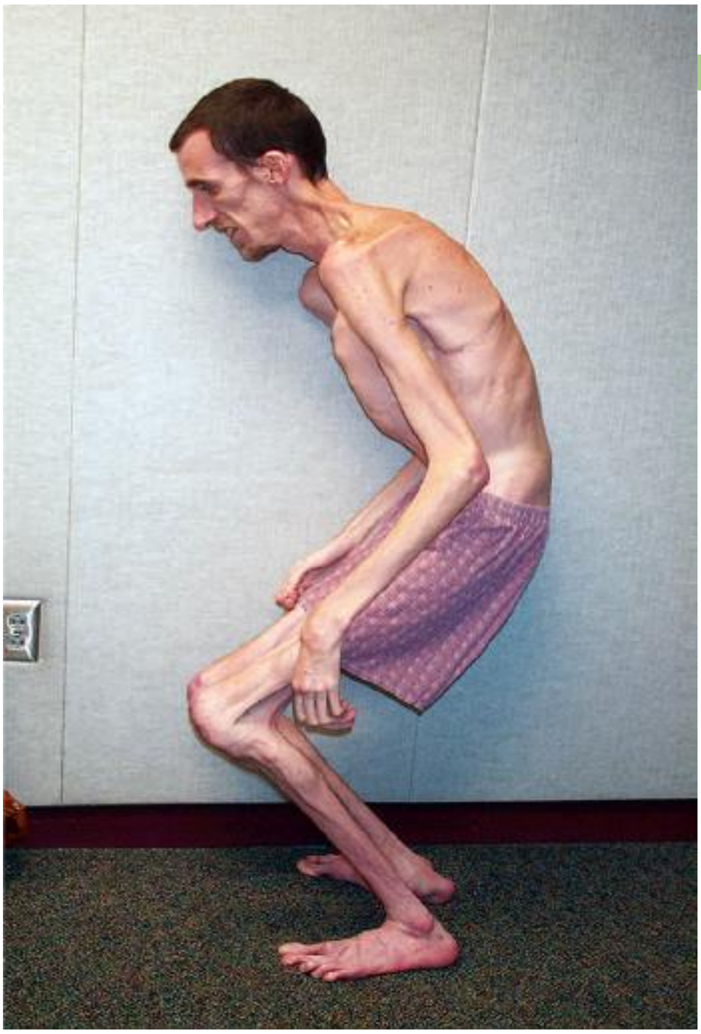
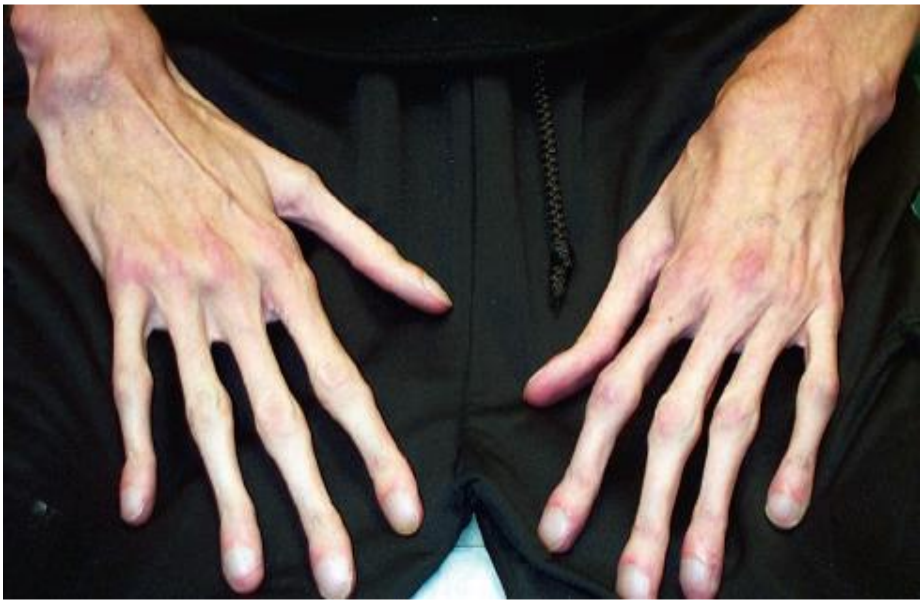
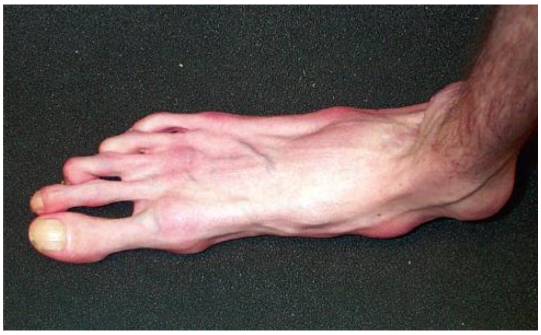
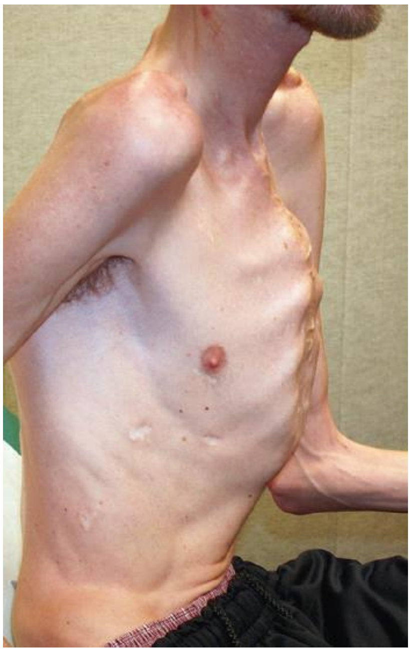
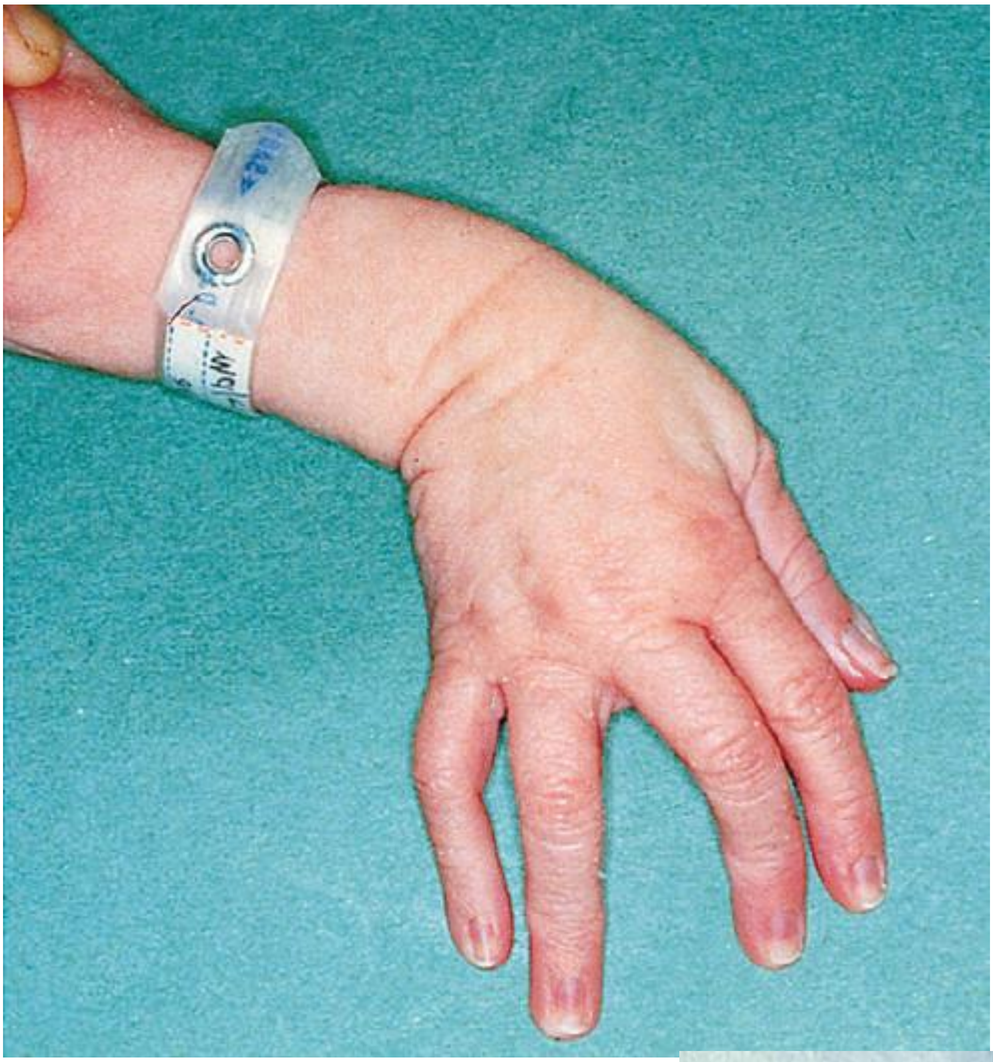
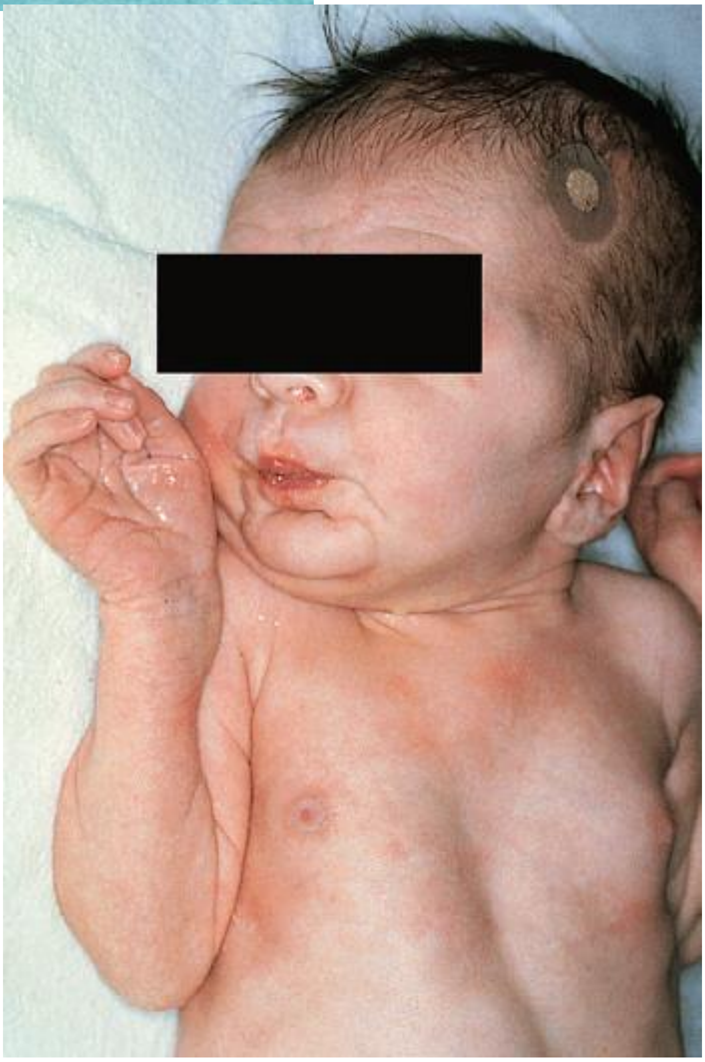






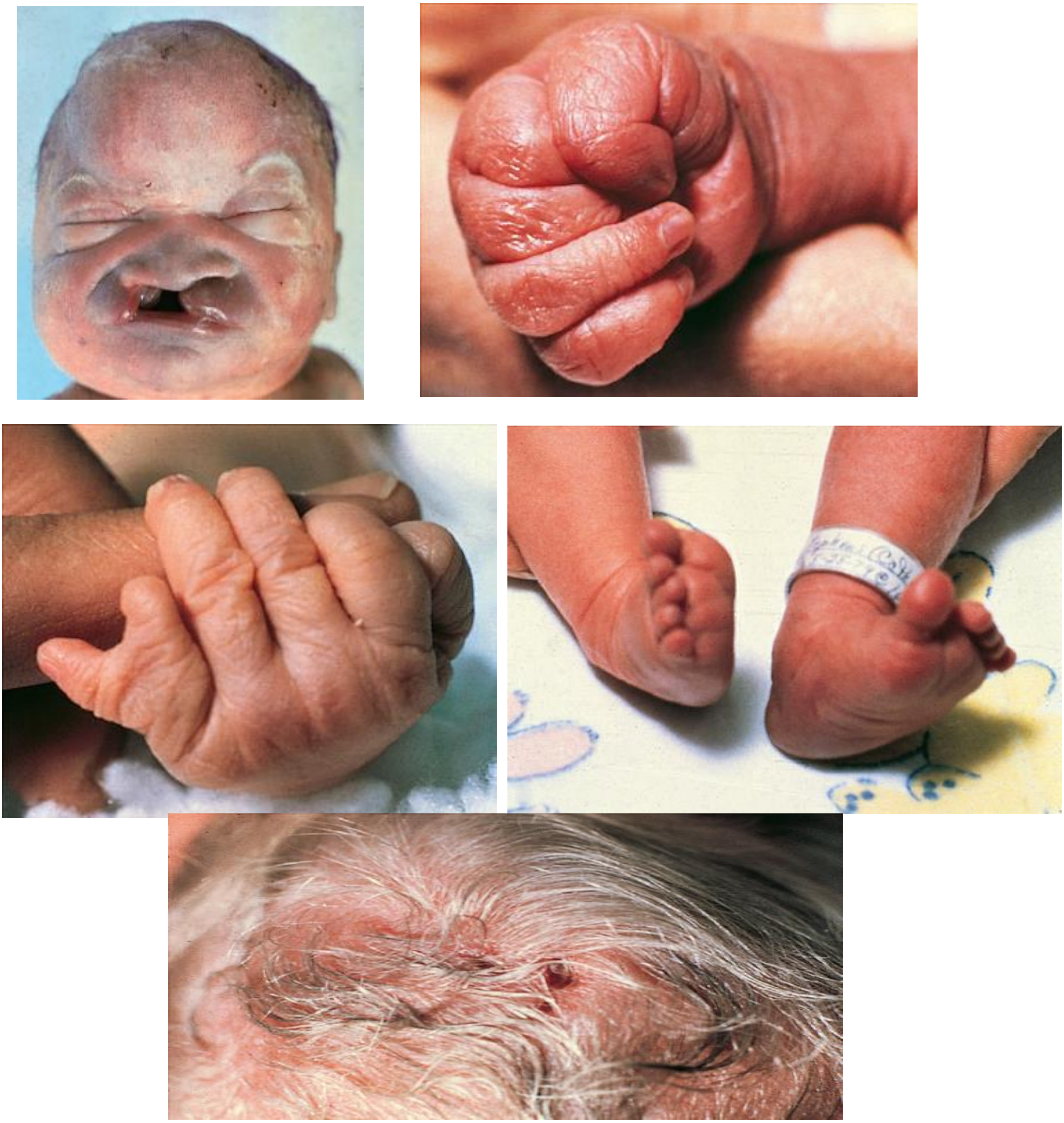






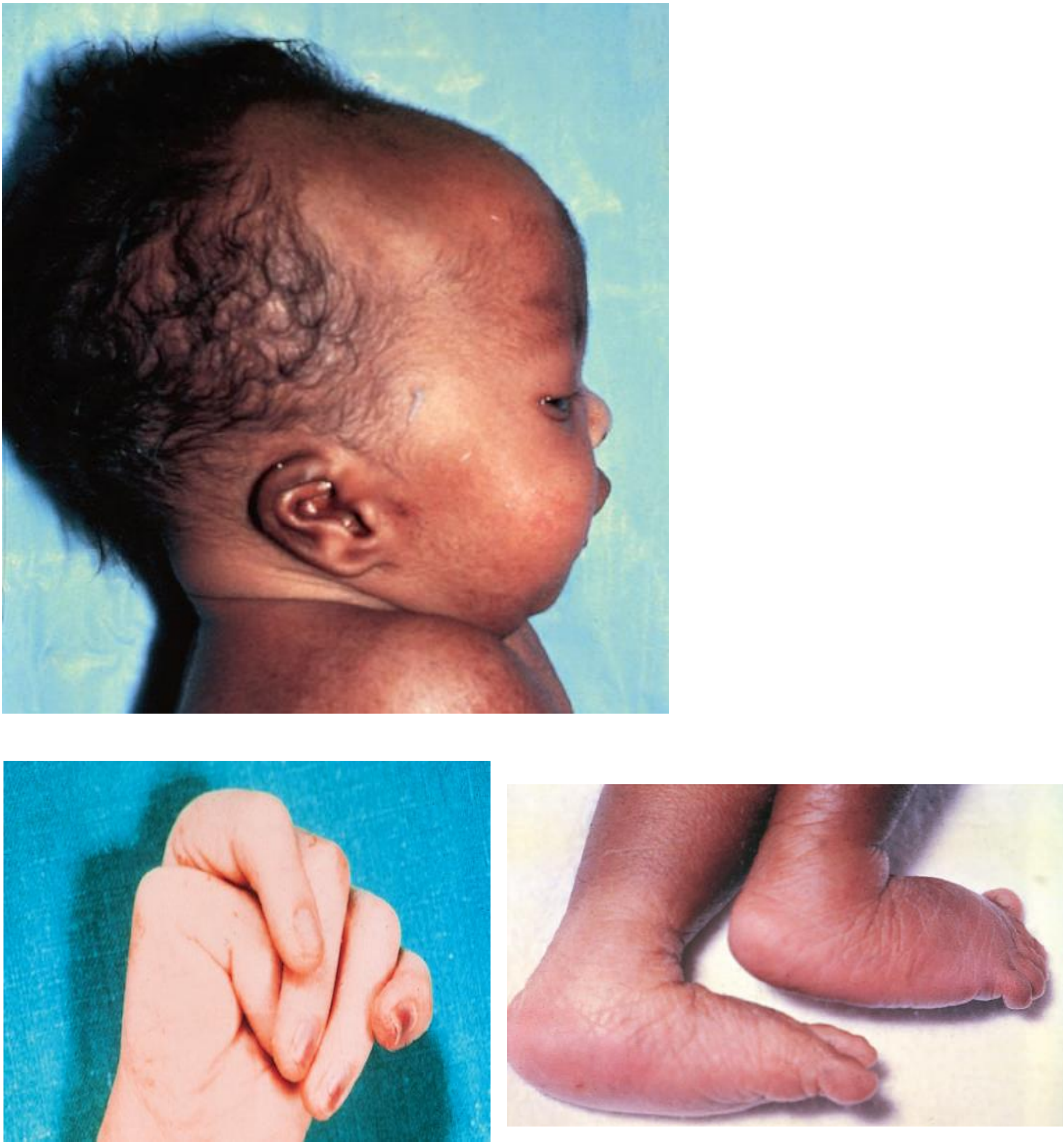
Trisomy 13

Several physical manifestations of trisomy 13. A, Facies showing midline defect. B, Clenched hand with overlapping fingers. C, Postaxial polydactyly. D, Equinovarus deformity. E, Typical punched-out scalp lesions of aplasia cutis congenita. *(A, Courtesy T. Kelly, MD, University of Virginia Medical Center, Charlottesville.* B *to* E, *Courtesy Kenneth Garver, MD, Pittsburgh, PA.)*



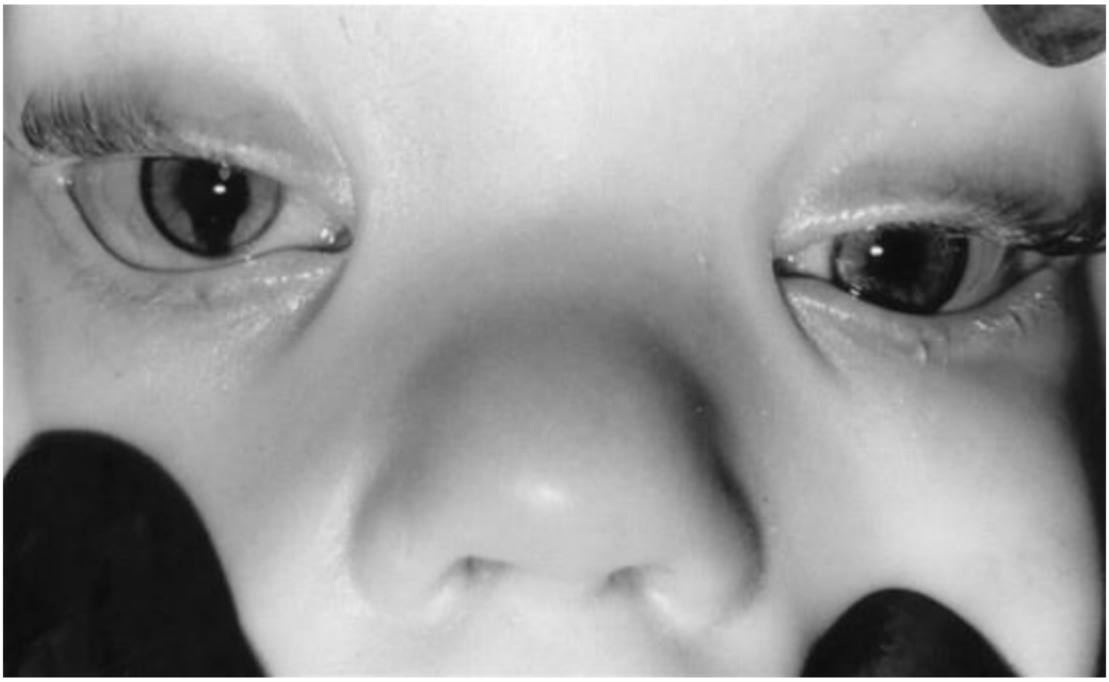
Trisomy 18

Several physical manifestations of trisomy 18. A, Typical profile reveals prominent occiput and low-set, posteriorly rotated malformed auricles. B, Clenched hand showing typical pattern of overlapping fingers. C, Rocker-bottom feet. ***(Courtesy Kenneth Garver, MD, Pittsburgh, PA.)***



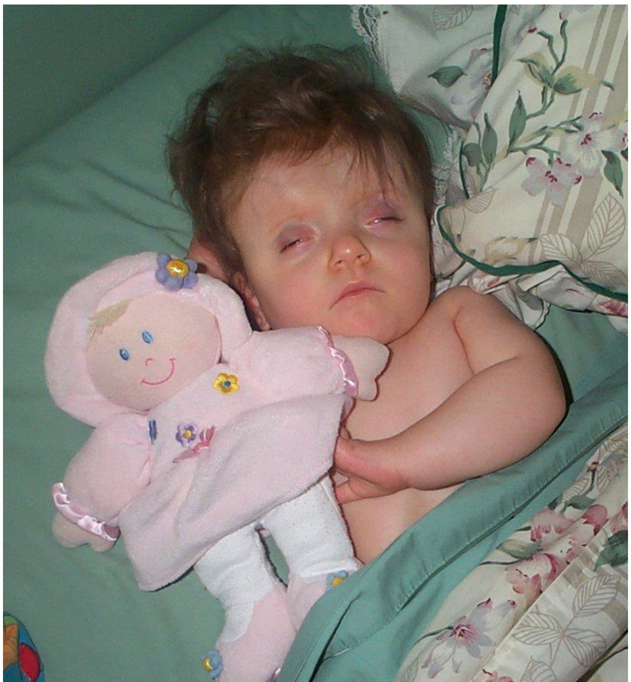
Cat Eye Syndrome

- **Iris coloboma**
- **Anal atresia (opening to the anus is missing)**
- **Skin tags or pits in front of the ears**
- **Unusually shaped ears**
- **Conductive hearing loss**
- **Hypertelorism (widely spaced eyes)**
- **Downward slanting palpebral fissures (outside corners of the eyes point downward)**
- **Strabismus**
- **Cleft lip and/or palate**
- **Congenital heart defects**
- **Urinary tract problems**
- **Skeletal abnormalities**
- **Developmental delay**
- **Mild to moderate intellectual disability**



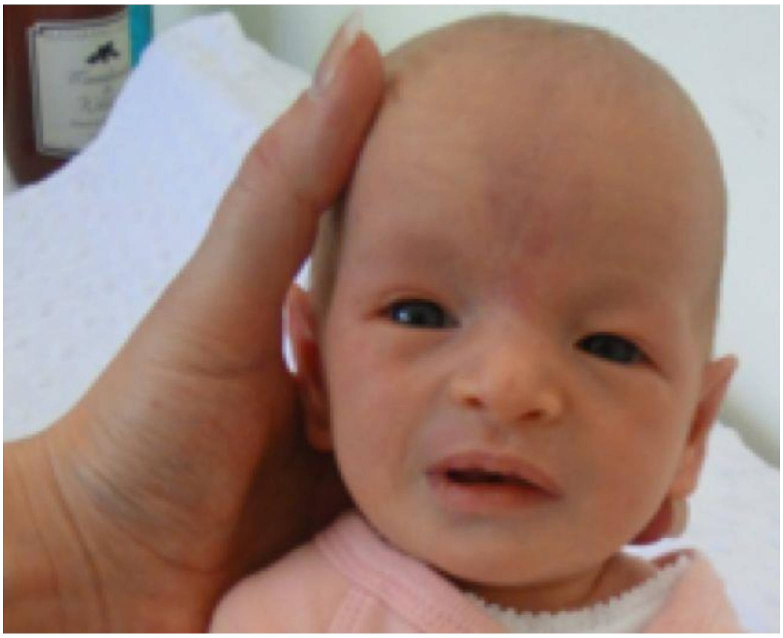
Triosmy 9

- Characteristic craniofacial features such as microcephaly (unusually small head); a sloping forehead with narrow temples; a broad nose with a bulbous tip and "slitlike" nostrils; a small jaw; abnormally wide fontanelles at birth; cleft lip and/or palate; low-set, misshapen ears; microphthalmia (unusually small eyes) and/or short, upwardly slanting eyelid folds (palpebral fissures)
- Different degrees of developmental delay and intellectual disability
- Abnormal growth including low birth weight, failure to thrive, hypotonia (low muscle tone), and short stature
- Vision problems
- Congenital heart defects
- Abnormalities of the muscles and/or bones such as congenital dislocation of the hips; abnormal position and/or limited function of the joints; underdevelopment of certain bones; and/or abnormal curvature of the spine
- Unusually formed feet, such as club foot or "rocker bottom" feet
- Abnormalities of the male reproductive system, including undescended testes, a small penis, and/or abnormal placement of the urinary opening
- Kidney problems
- Brain malformations such as hydrocephalus and/or Dandy-Walker malformation

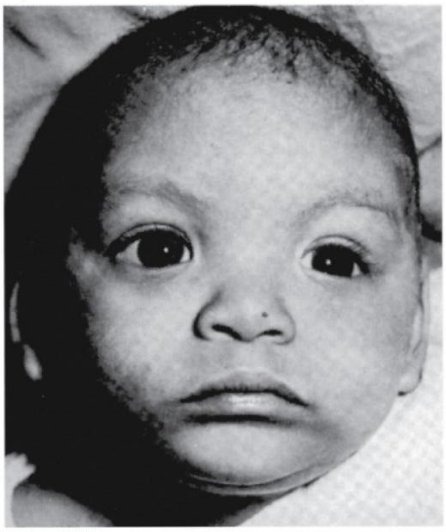


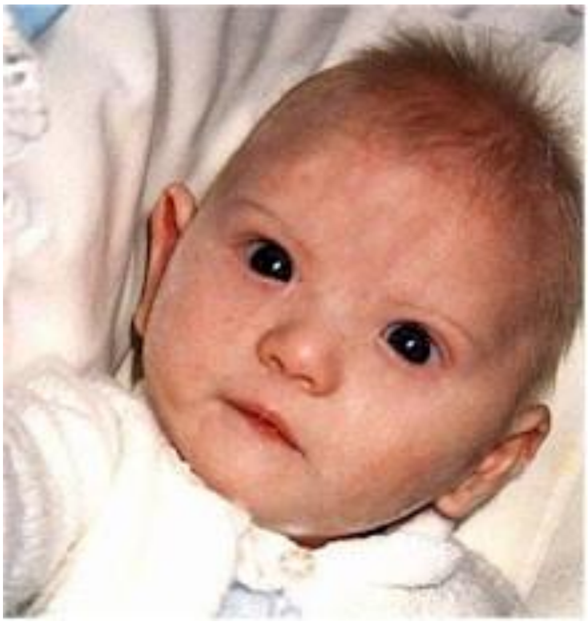
Deletion 5p (cri du chat syndrome)

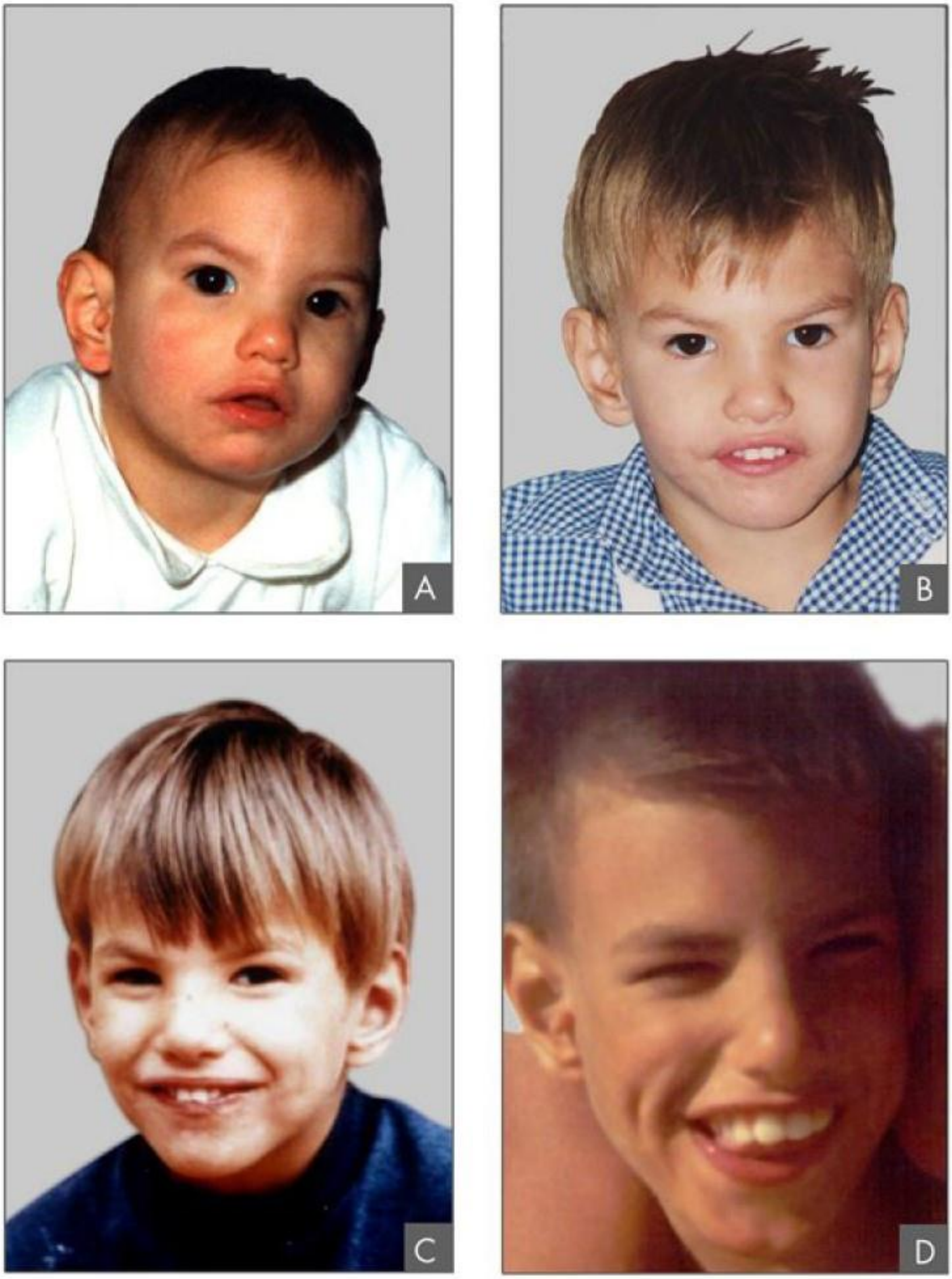
The main features are hypotonia, short stature, characteristic shrill cry in the first few weeks of life (cat-like cry), microcephaly with protruding metopic suture, hypertelorism, bilateral epicanthic folds, high arched palate, wide and flat nasal bridge, and intellectual disability



b) Individual with Cri-du-chat syndrome

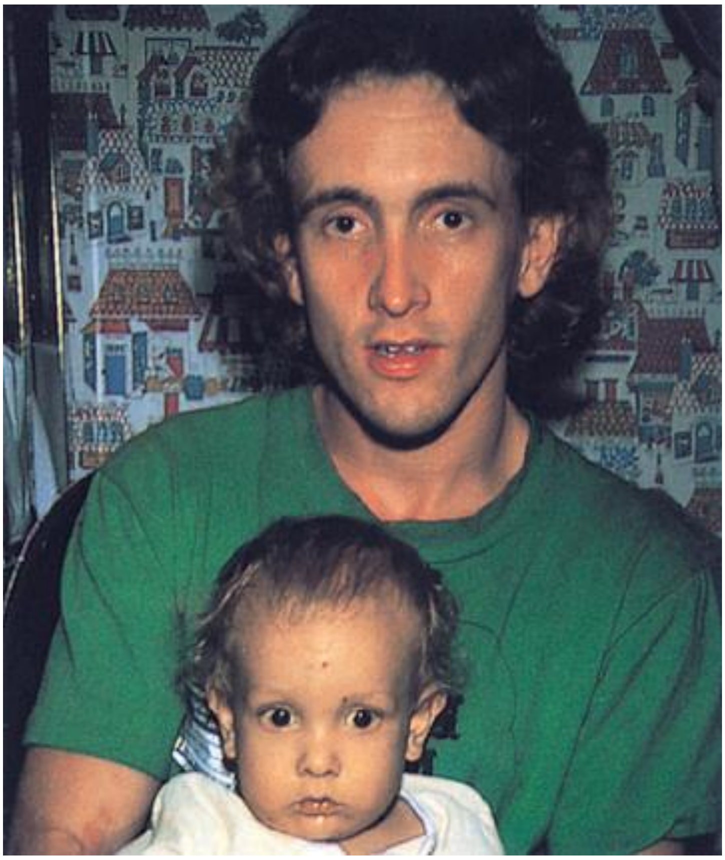


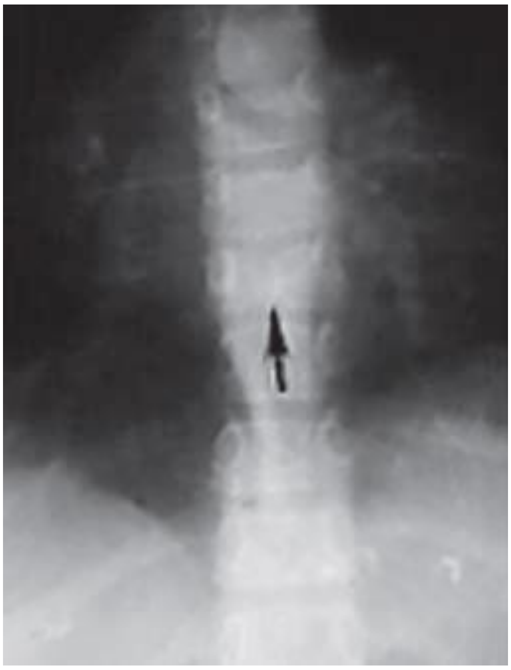


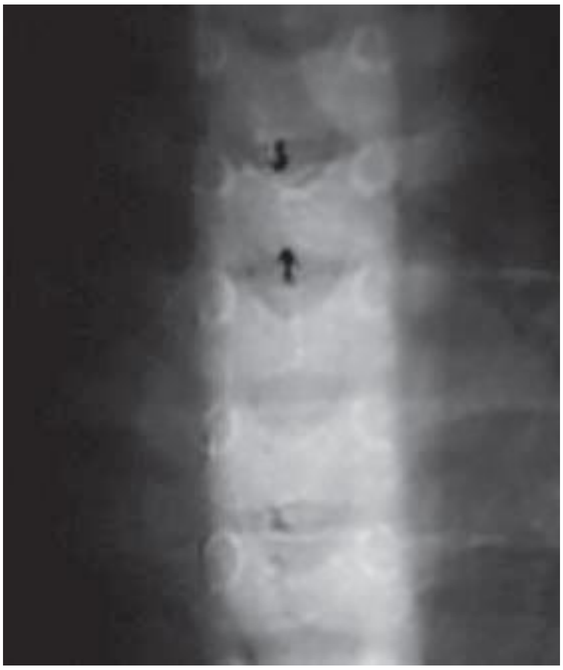

A
B
C
D

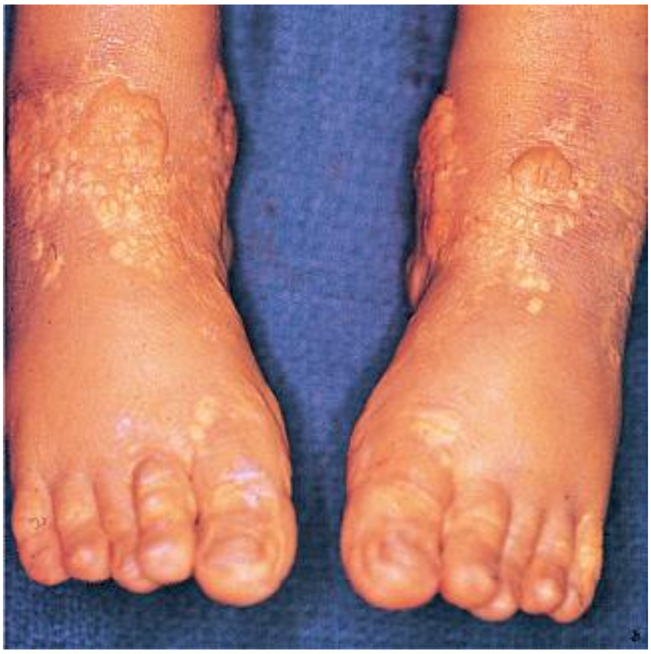
Alagille syndrome

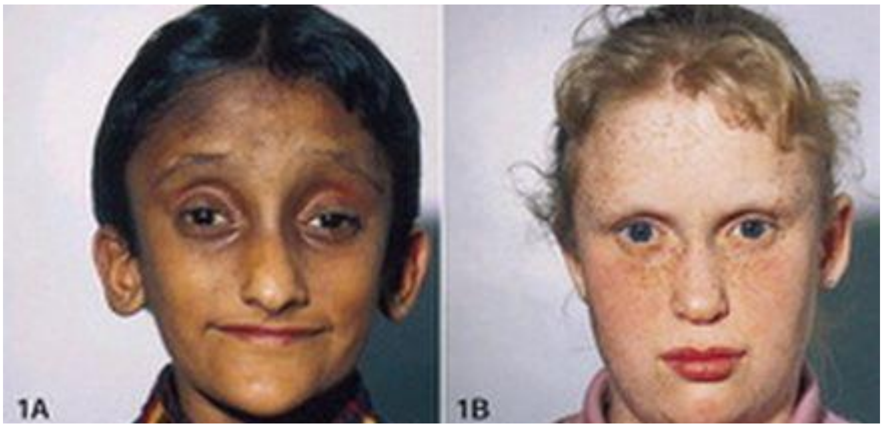
Disease features include paucity of intrahepatic bile ducts leading to cholestatic jaundice, unusual facies (wide forehead, deep-set eyes, long straight nose, prominent chin, small, low-set ears, posterior embryotoxon, vertebral defects, and pulmonary artery hypoplasia. Children with this condition have high circulating concentrations of total cholesterol, phospholipids, triglycerides, pre-β- and β-lipoproteins, and elevated apolipoproteins. Thus, large lipid accumulations in the skin and other tissues are common







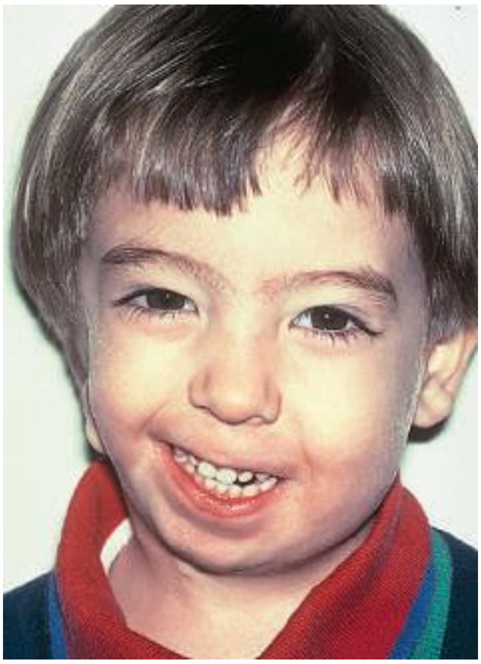



1A
1B

Oculo-Auriculo-Vertebral Spectrum (Goldenhar Syndrome and Craniofacial or Hemifacial Microsomia)

Craniofacial

Facial asymmetry
Unilateral maxillary, temporal, and zygomatic hypoplasia
Epibulbar dermoids with fine hairs
Unilateral colobomas of upper eyelids
Esotropia or exotropia
Preauricular appendages
Pretragal fistula
External ear deformities
External auditory canal stenosis or atresia
Conductive hearing deficits
Macrostomia due to mandibular dysgenesis
Lateral facial cleft
Cleft lip with or without cleft palate

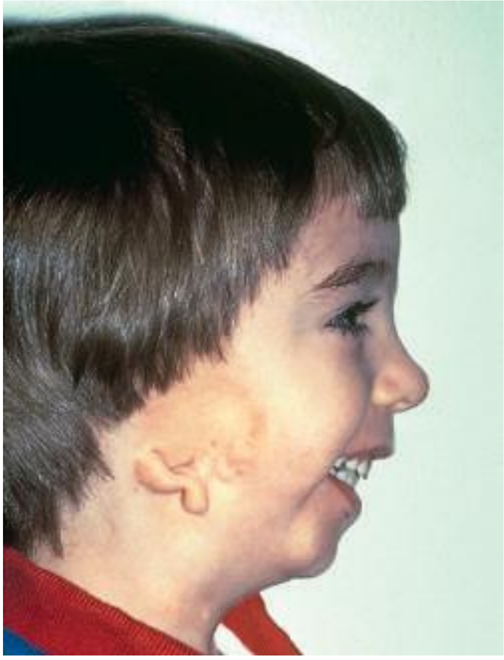


Central Nervous System

Seventh cranial nerve (CN) palsy
Microcephaly
Hydrocephaly
Encephaloceles

Extracranial Skeletal

Cervical vertebral fusion
Spina bifida
Hemivertebrae
Butterfly, fused, or hypoplastic vertebrae
Scoliosis
Rib anomalies

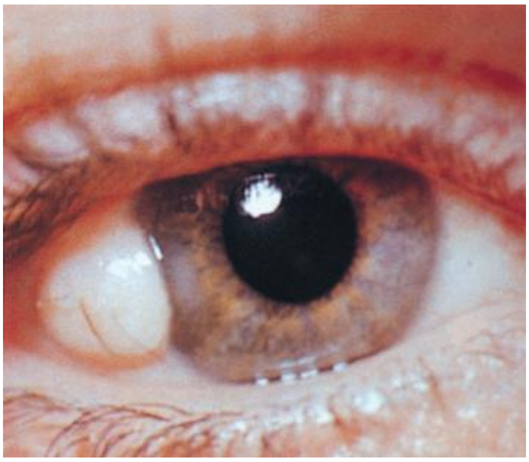


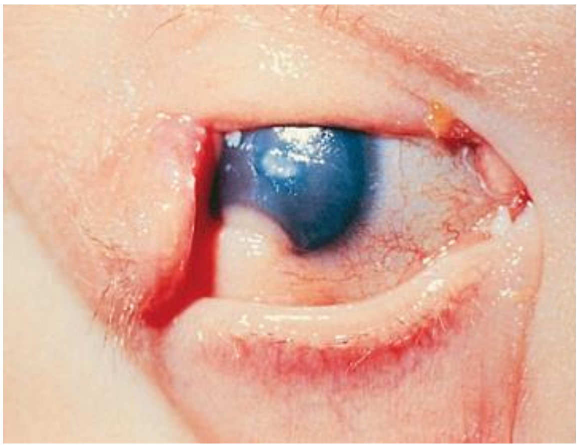
Cardiovascular

Ventricular septal defect
Tetralogy of Fallot
Transposition of the great vessels
Coarctation of the aorta
Pulmonic stenosis
Dextrocardia

Other

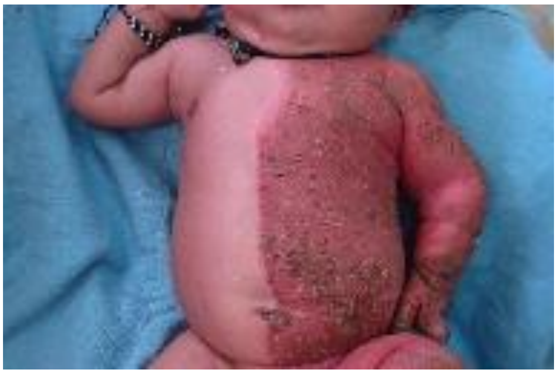
Pulmonary dysplasia
Tracheoesophageal fistula
Renal anomalies
Imperforate anus

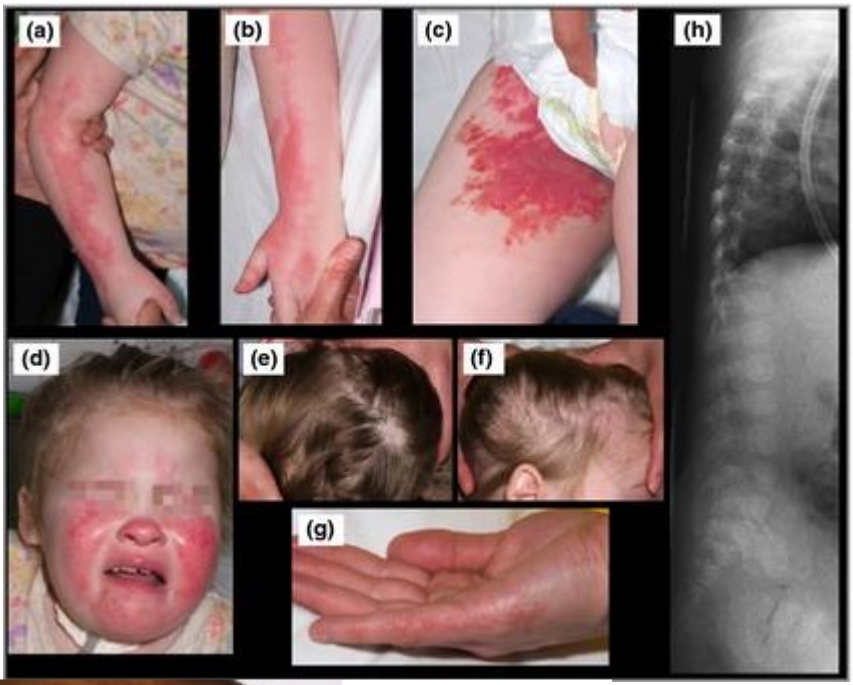




CHILD (congenital hemidysplasia with ichthyosiform erythroderma, limb defects

X-linked dominant disorder caused by heterozygous loss of function mutations in *NSDHL*
Unilateral ichthyosiform skin lesions with sharp midline demarcation
Psychotropic skin lesions
Verruciform xanthoma
Hyperkeratosis, parakeratosis and acanthosis
Congenital hemidysplasia
Ipsilateral limb defects
Visceral malformations
CNS anomalies





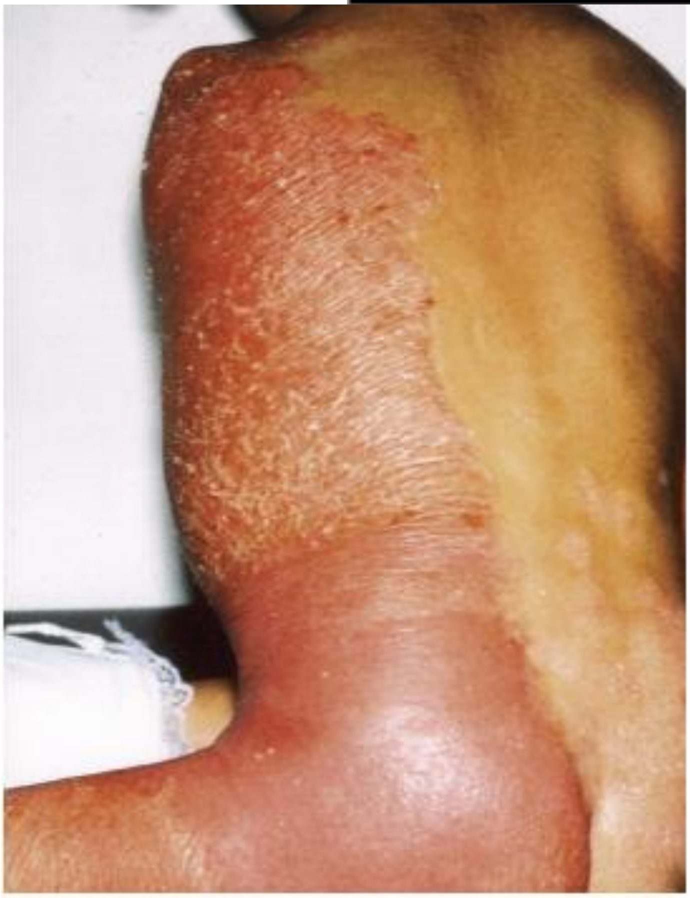
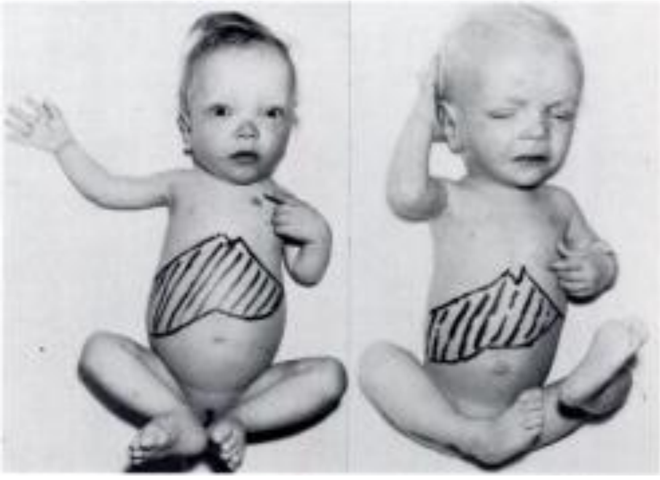


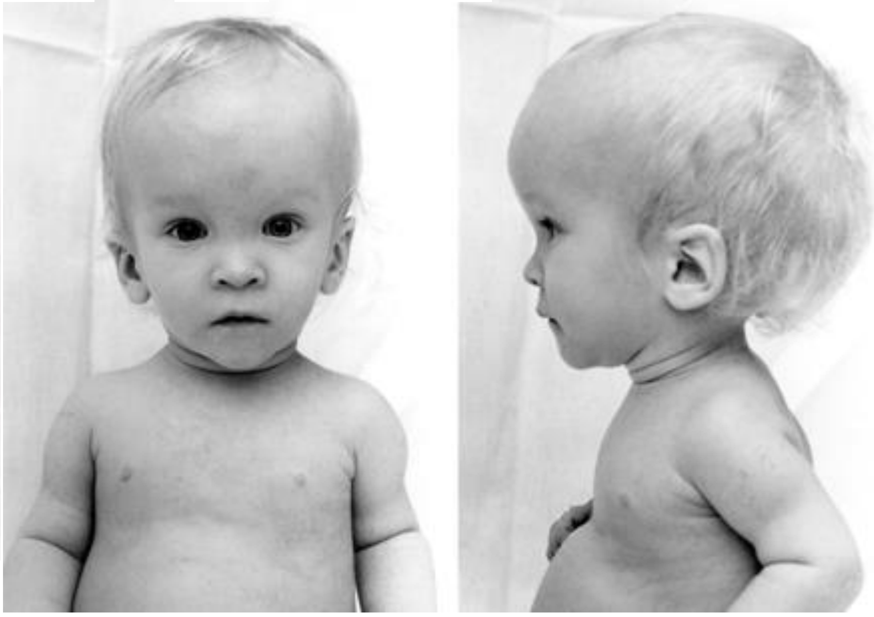
FIGURE 5: Erythematous desquamative lesion associated to upper limb agenesis on the same hemibody

Mulibrey Nanism

Profound growth delays and distinctive abnormalities of the muscles, liver, brain, and eyes. The acronym mulibrey stands for (mu)scle, (li)ver, (br)ain, and (ey)e; nanism is another word for dwarfism. Signs and symptoms of the disorder may include constrictive pericarditis; low birth weight; short stature; severe progressive growth delays; hypotonia; hepatomegaly; and yellow discoloration of the eyes in infancy. scaphocephaly, facial triangularity, high and broad forehead, and low nasal bridge

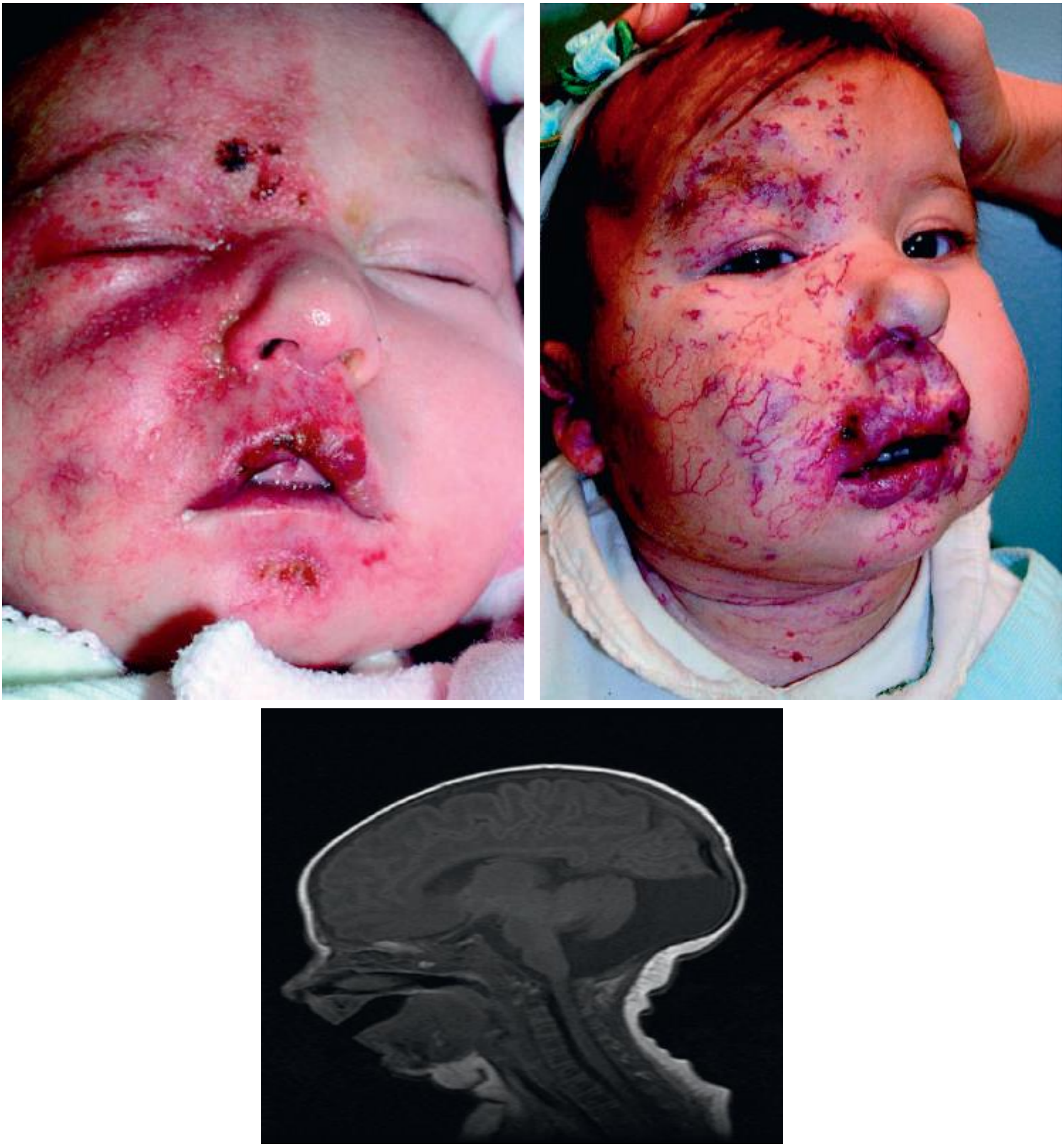
It is caused by mutations in the *trim37* gene and is inherited in an autosomal recessive manner.





PHACES (posterior fossa malformations, hemangiomas, arterial anomalies, cardiac defects, eye anomalies, sternal clefting) syndrome

PHACES syndrome. A, At birth lesion are plaque-like and may mimic a port-wine stain. B, However once they start to rapidly proliferate, becoming raised, as seen in the same infant at 1 year old. C, This magnetic resonance imaging (MRI) reveals a Dandy-Walker malformation in an infant with PHACES.



Congenital Rubella Syndrome

Cardiovascular
Patent ductus arteriosus
Pulmonary artery stenosis
Ventriculoseptal defect
Myocarditis

Central nervous system
Chronic meningitis
Parenchymal necrosis
Vasculitis with calcification

Eye
Microphthalmia
Cataract
Iridocyclitis
Ciliary body necrosis
Glaucoma
Retinopathy

Ear
Cochlear hemorrhage
Endothelial necrosis

Lung
Chronic mononuclear interstitial pneumonitis

Liver
Hepatic giant cell transformation
Fibrosis
Lobular disarray
Bile stasis

Kidney
Interstitial nephritis

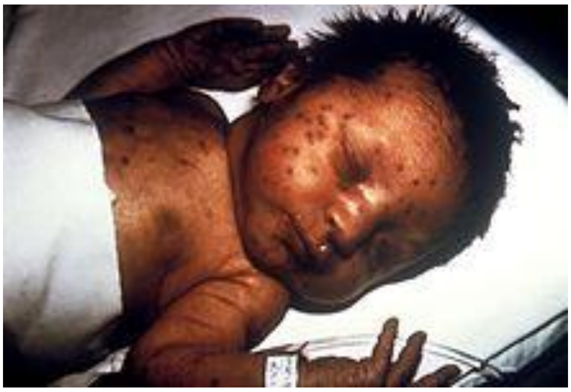
Adrenal gland
Cortical cytomegaly

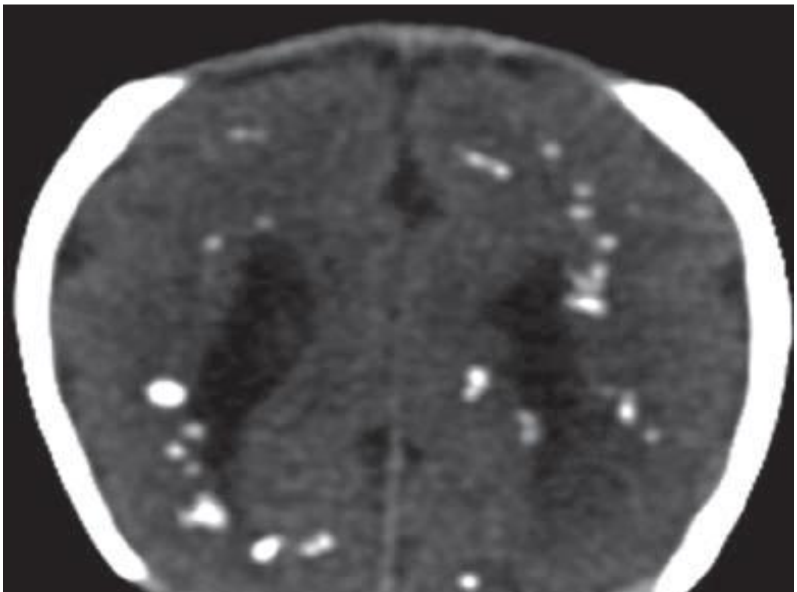
Bone
Malformed osteoid
Poor mineralization of osteoid
Thinning cartilage

Spleen, lymph node
Extramedullary hematopoiesis

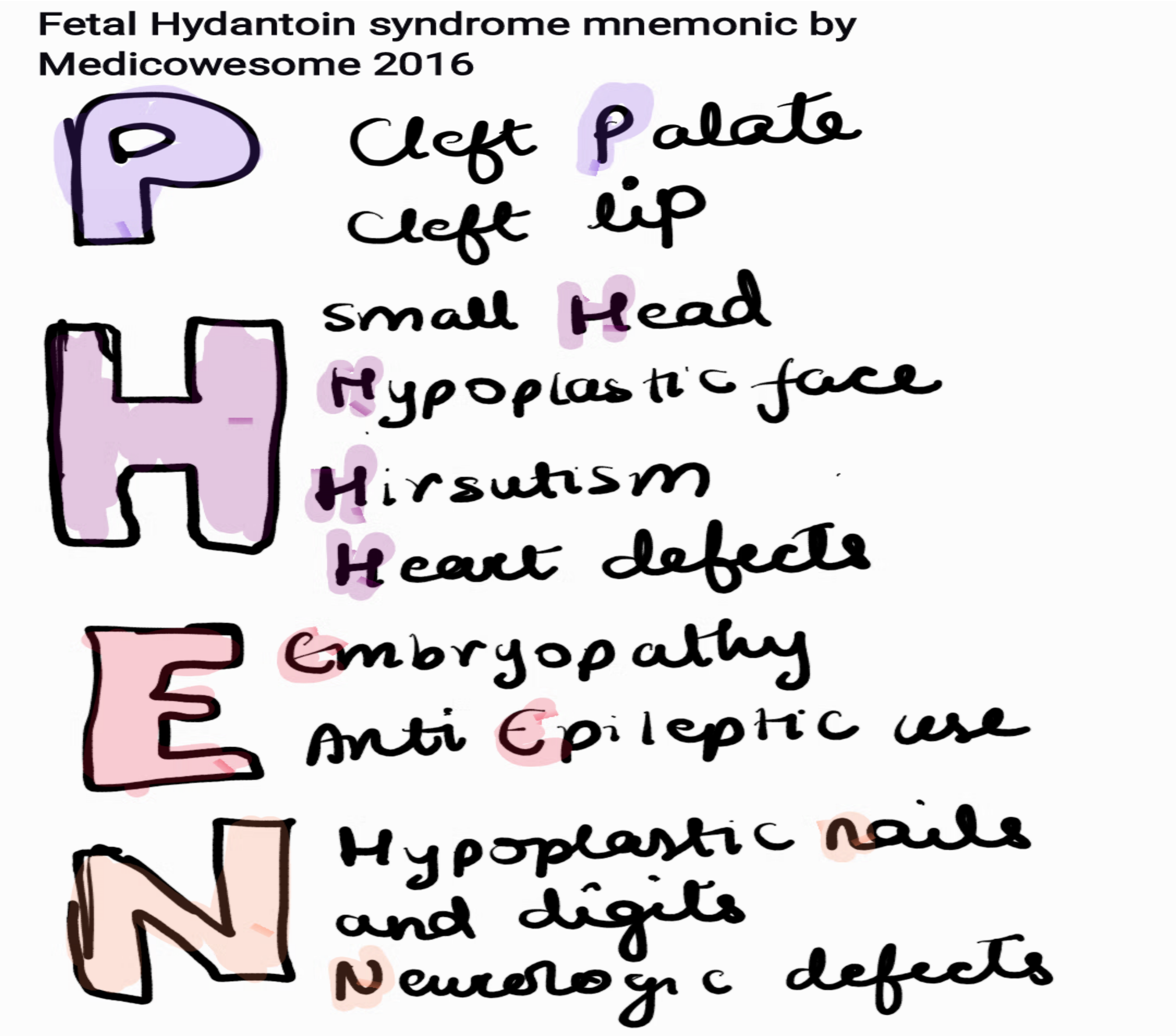
Thymus
Histiocytic reaction
Absence of germinal centers

Skin
Erythropoiesis in dermis





Fetal hydantoin syndrome



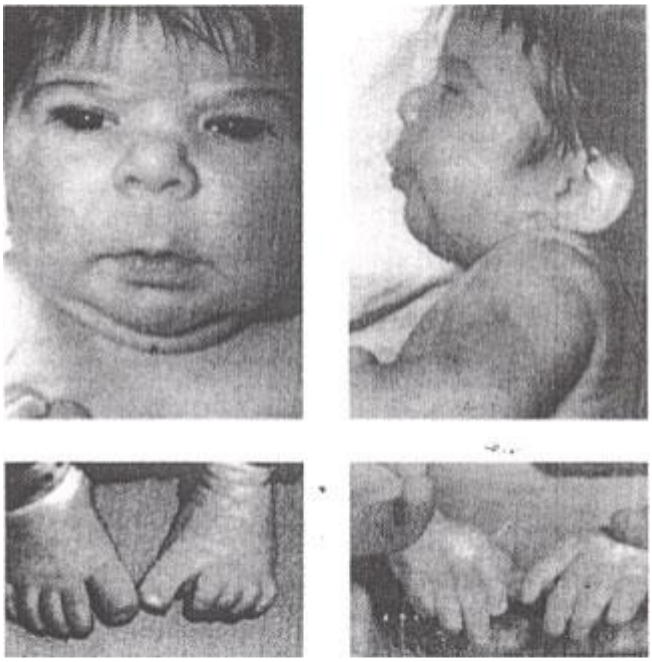
Fetal Hydantoin syndrome mnemonic by Medicowesome 2016

P
Cleft Palate
Cleft lip

H
small Head
Hypoplastic face
Hirsutism
Heart defects

E
Embryopathy
Anti Epileptic use

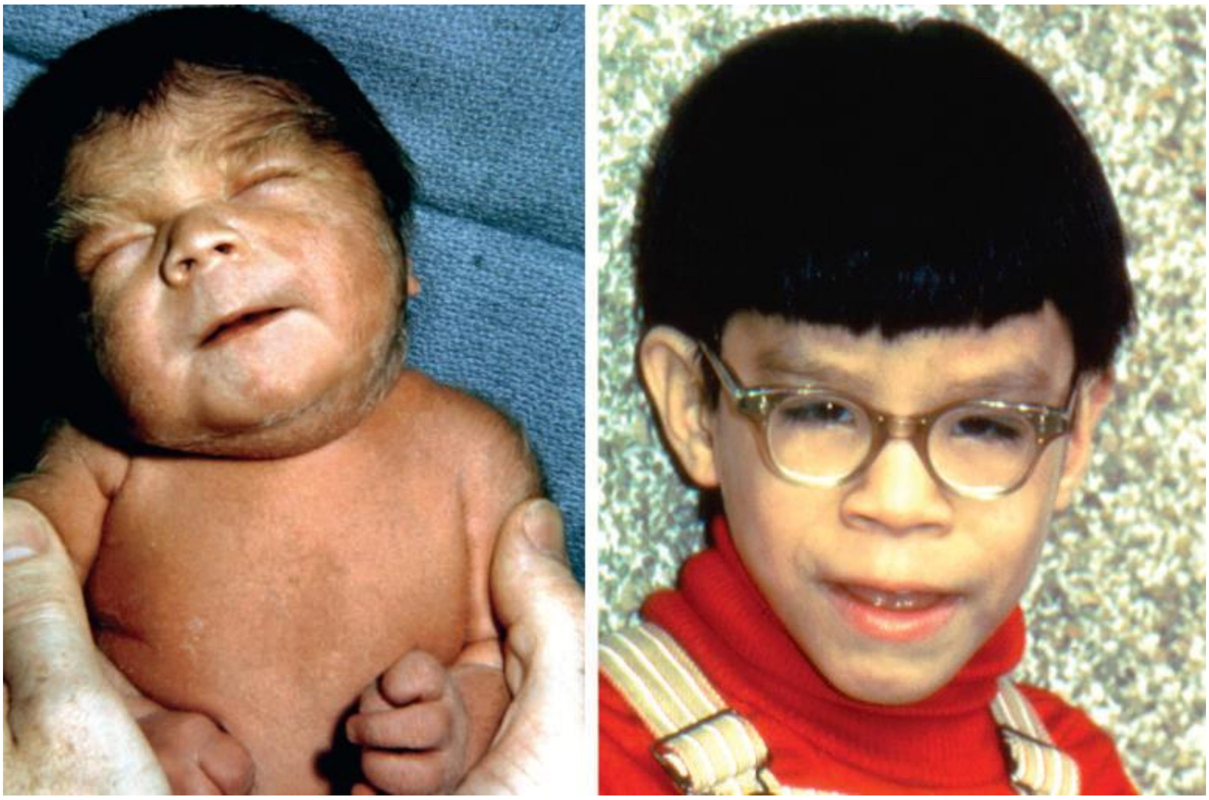
N
Hypoplastic nails and digits
Neurologic defects



Fetal Alcohol Syndrome

(a) Prenatal onsetand persistence of growth deficiency for length, weight, and head circumference;

(b) Facial abnormalities, including short palpebral fissures, epicanthal folds, maxillary hypoplasia, micrognathia, smooth philtrum, and a thin, smooth upper lip.
(c) Cardiac defects, primarily septal defects;
(d) Minor joint and limb abnormalities, including some restriction of movement and altered palmar crease
(e) Patterns
(f) Delay of development and mental deficiency varying from borderline to severe



Inherited Pancytopenia Syndromes

Fanconi anemia

Shwachman-Diamond syndrome

Dyskeratosis congenita

Congenital amegakaryocytic thrombocytopenia

Reticular dysgenesis

Unclassified inherited bone marrow failure syndromes

Other genetic syndromes

Down syndrome

Dubowitz syndrome

Seckel syndrome

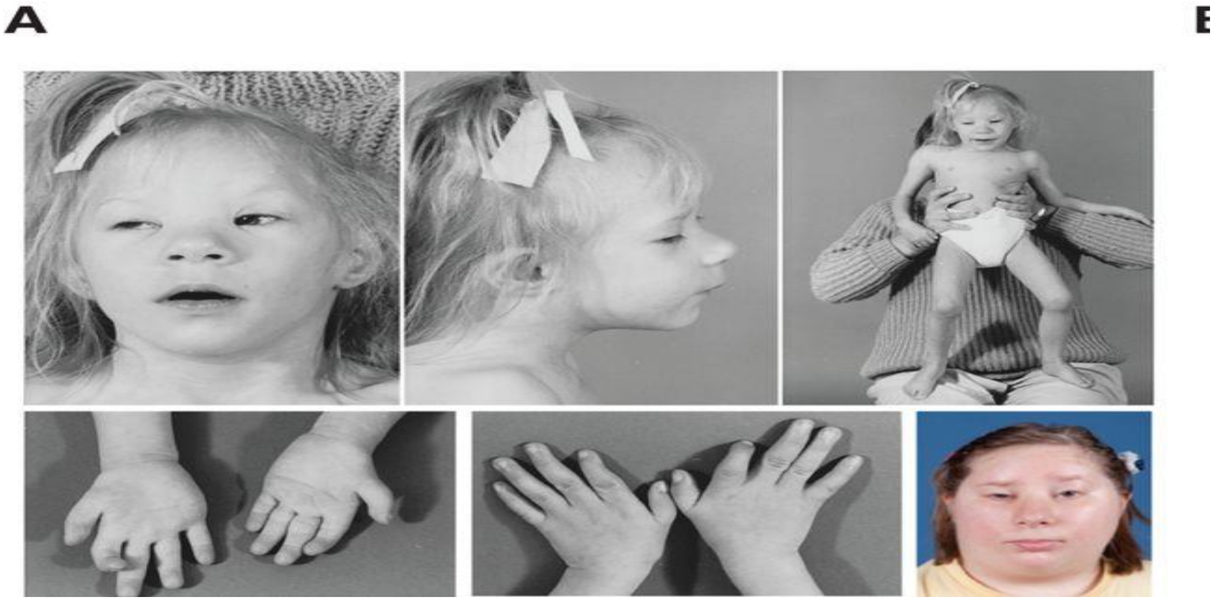
Schimke immunoosseous dysplasia

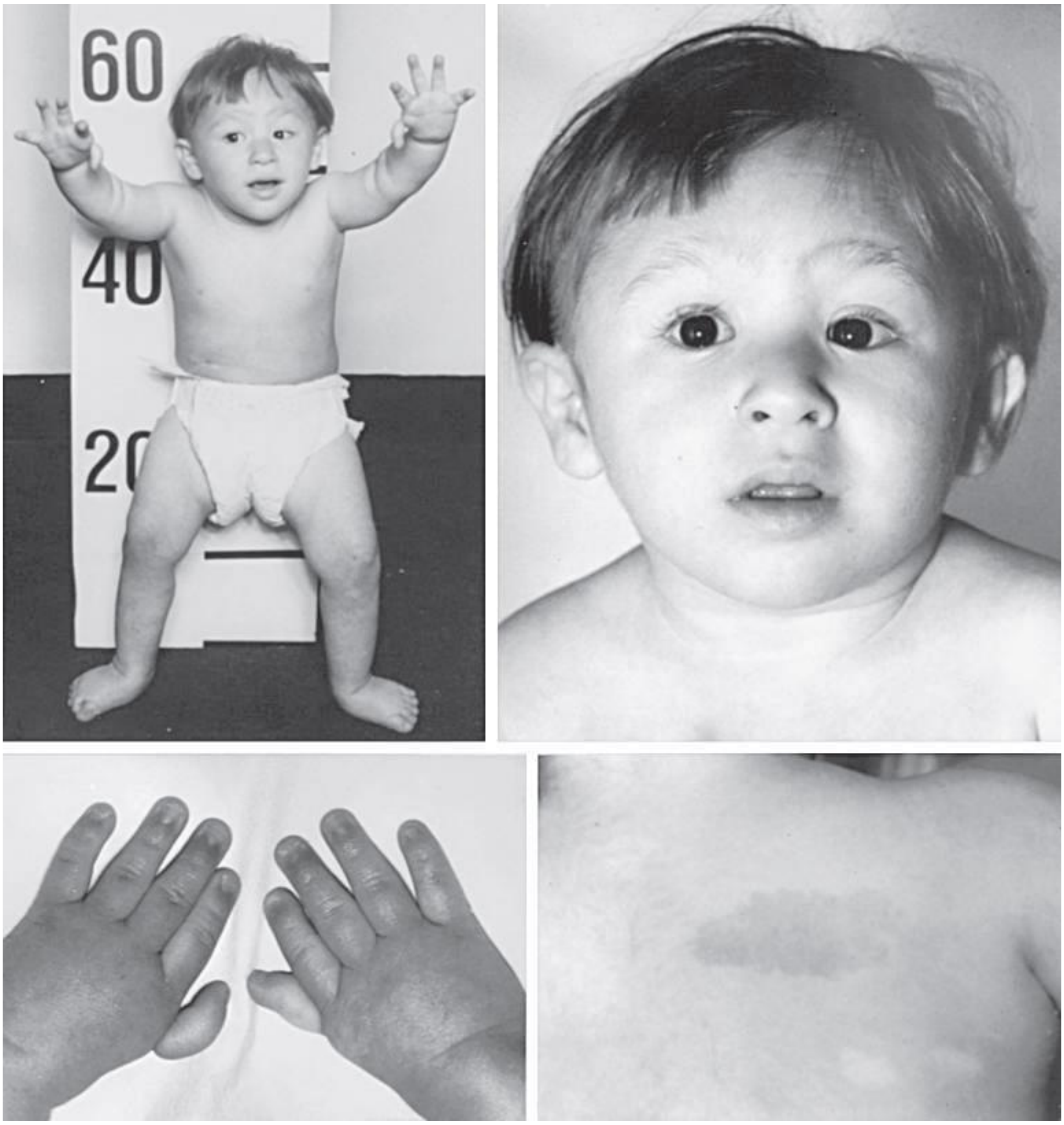
Cartilage-hair hypoplasia

Noonan syndrome

Fanconi Anemia

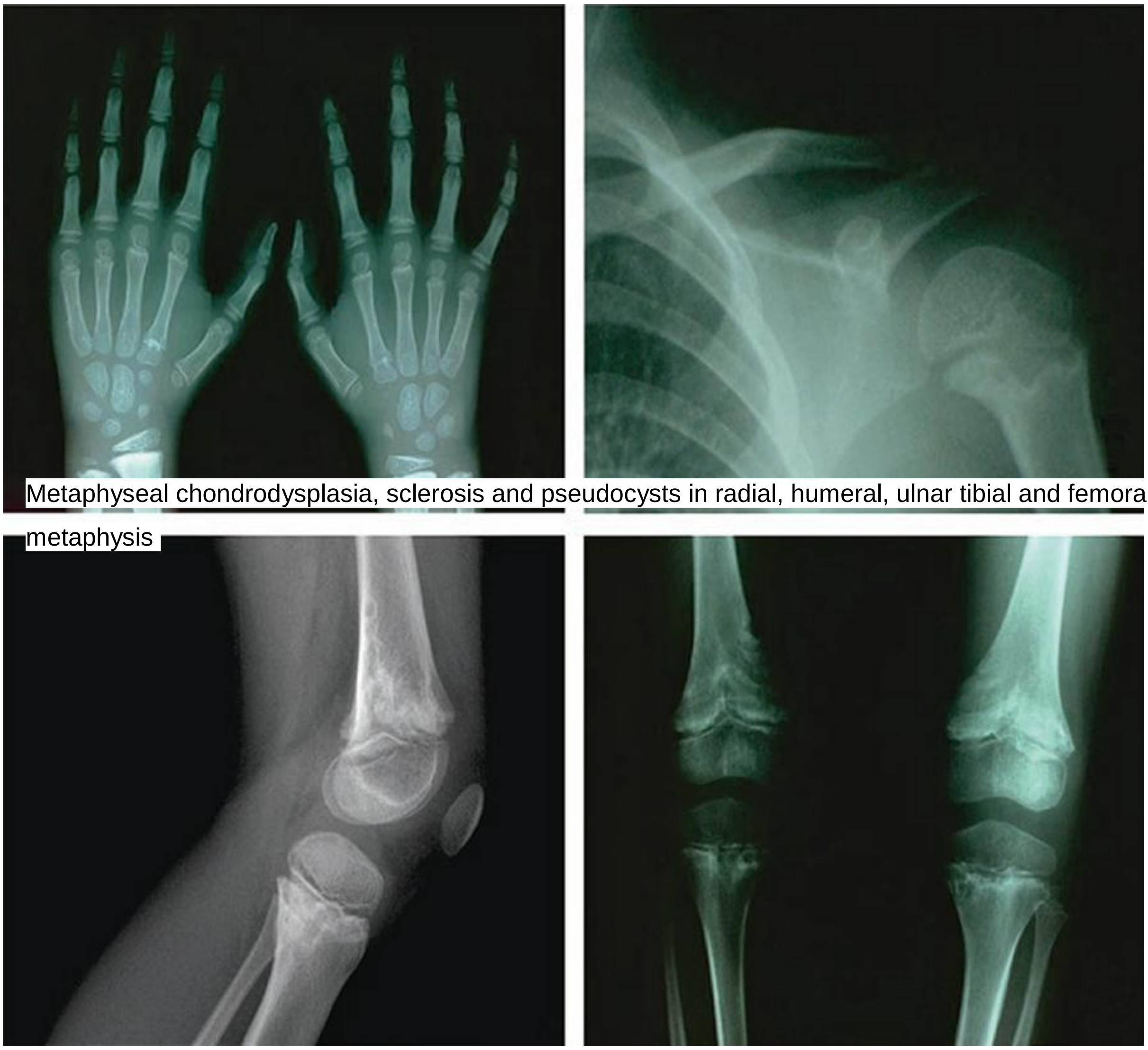
Skin pigment changes ± café-au-lait spots
Short stature
Upper limb abnormalities (thumbs, hands, radii, ulnas)
Hypogonadal and genital changes (mostly male)
Other skeletal findings (head/face, neck, spine)
Eye/lid/epicanthal fold anomalies
Renal malformations
Gastrointestinal/cardiopulmonary malformations
Hip, leg, foot, toe abnormalities
Ear anomalies (external and internal), deafness




60
40

Shwachman-Diamond syndrome

Shwachman-Diamond syndrome is typically characterized by signs of insufficient absorption (malabsorption) of fats and other nutrients due to abnormal development of the pancreas (pancreatic insufficiency) and impaired functioning of the bone marrow, resulting in low levels of circulating blood cells (hematologic abnormalities). Additional characteristic findings may include short stature; abnormal bone development affecting the rib cage and/or bones in the arms and/or legs (metaphyseal dysostosis); recurrent infections; and/or liver dysfunction.



Metaphyseal chondrodysplasia, sclerosis and pseudocysts in radial, humeral, ulnar tibial and femoral metaphysis

Dyskeratosis Congenita

Lacy reticular pigmentation of skin dystrophic fingernails and toenails,premature graying of hair, hair loss, short stature, oral leukoplakia, squamous cell cancer of head and neck, pulmonary fibrosis, osteopenia, hypogonadism.

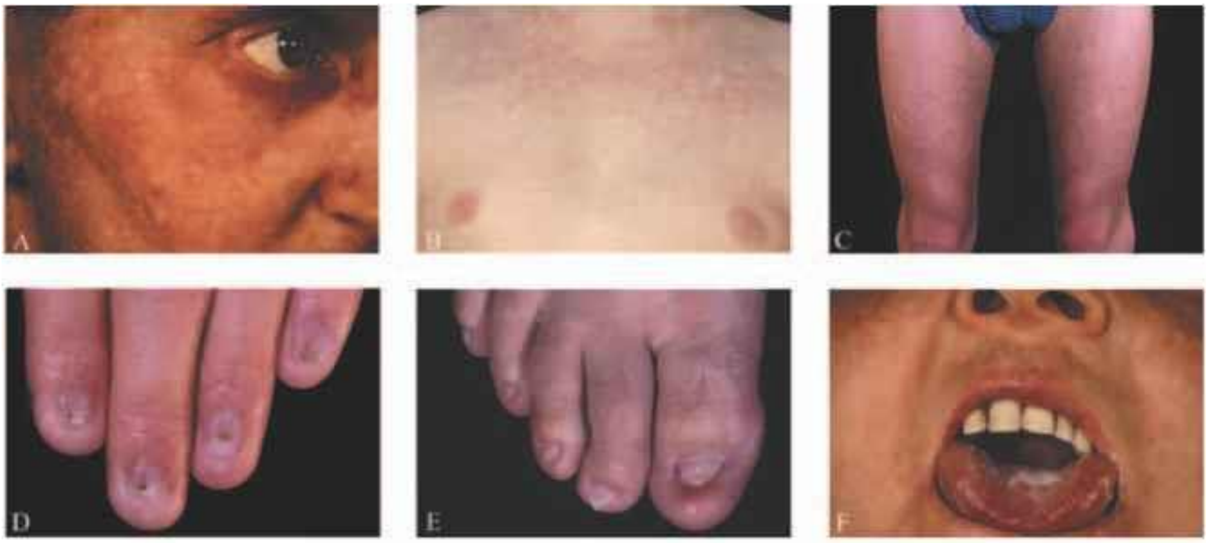
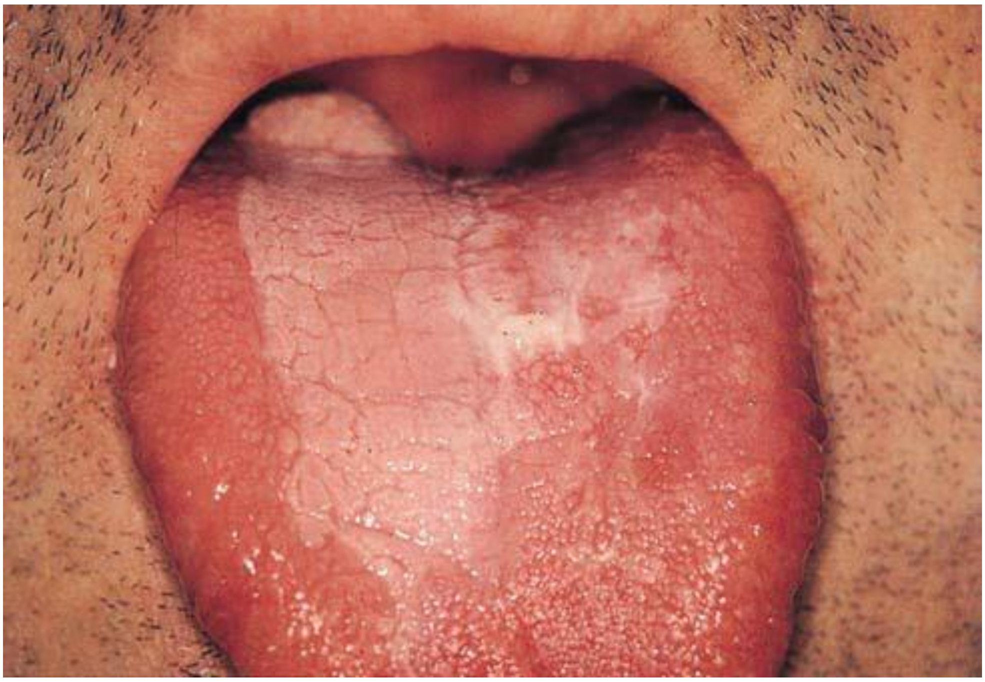


Figure 12.4 Photographs of DC patients showing abnormal skin pigmentation (A, B, C), nail dystrophy (D, E) and leucoplakia of tongue (F).

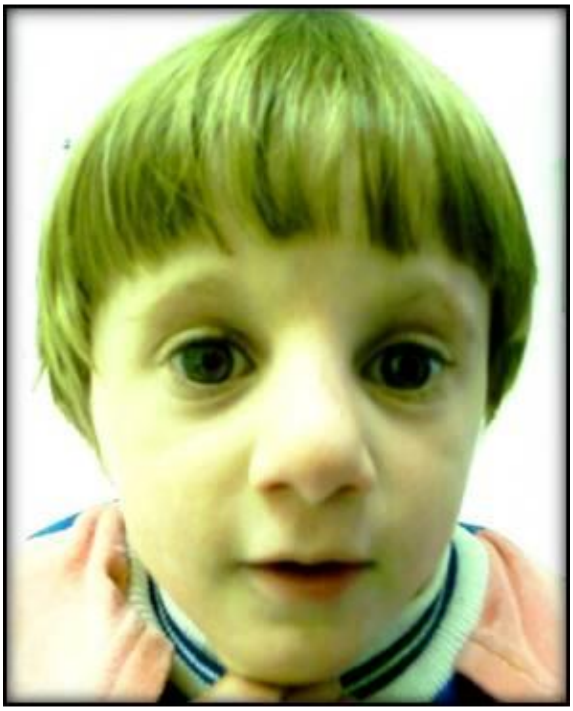


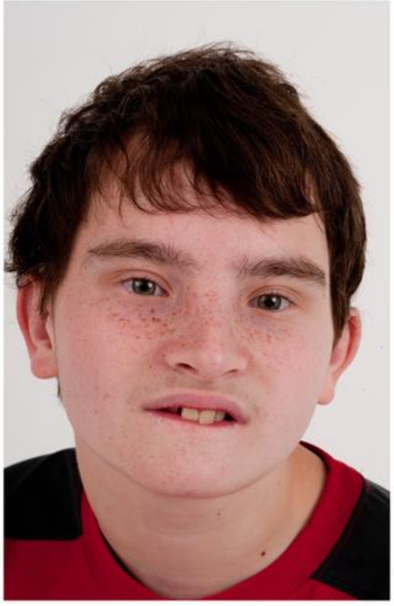
Dubowitz Syndrome

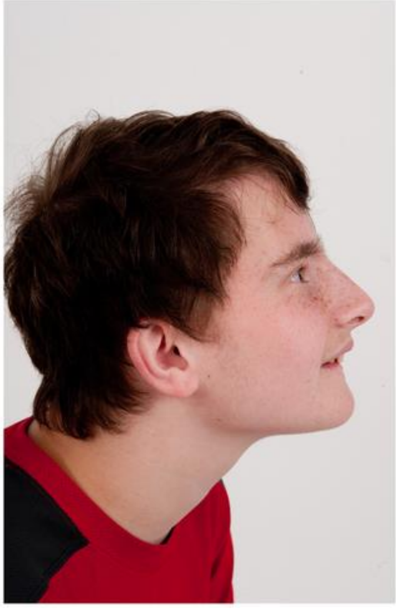
Dubowitz syndrome is an autosomal recessive disorder characterized by a peculiar facies, infantile eczema, small stature, and mild microcephaly. The face is small, with a shallow supraorbital ridge, a nasal bridge at the same level as the forehead, short palpebral fissures, variable ptosis, and micrognathia. There is a predilection to cancer as well as to bone marrow dysfunction in these patients. Approximately 10% of patients have hematopoietic disorders including moderate pancytopenia, hypoplastic anemia, bone marrow hypoplasia, and full-blown aplastic anemia. No gene mutation has been identifie

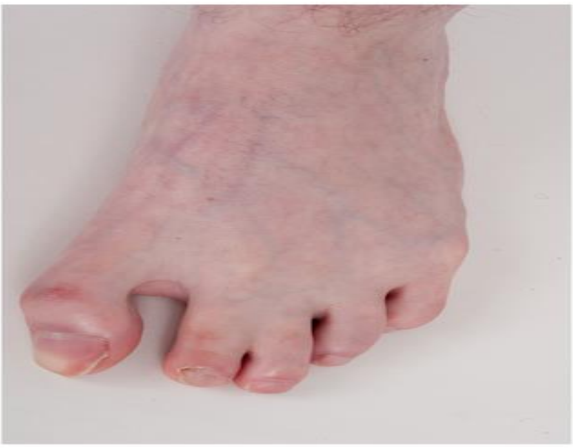
Facial features of DS

- Triangular-shaped face (with chin as bottom point; see photo of girl)
- Epicanthal folds (skin covering the inner corners of eyelids)
- Flat brow ridges (bone directly over eyes is smooth)
- Receding/underdeveloped jaw
- Ptosis (droopy upper eyelid)
- Sparse or absent eyebrows
- Sparse or thin head hair
- Malformed ears
- Low-set ears
- Wide-set eyes



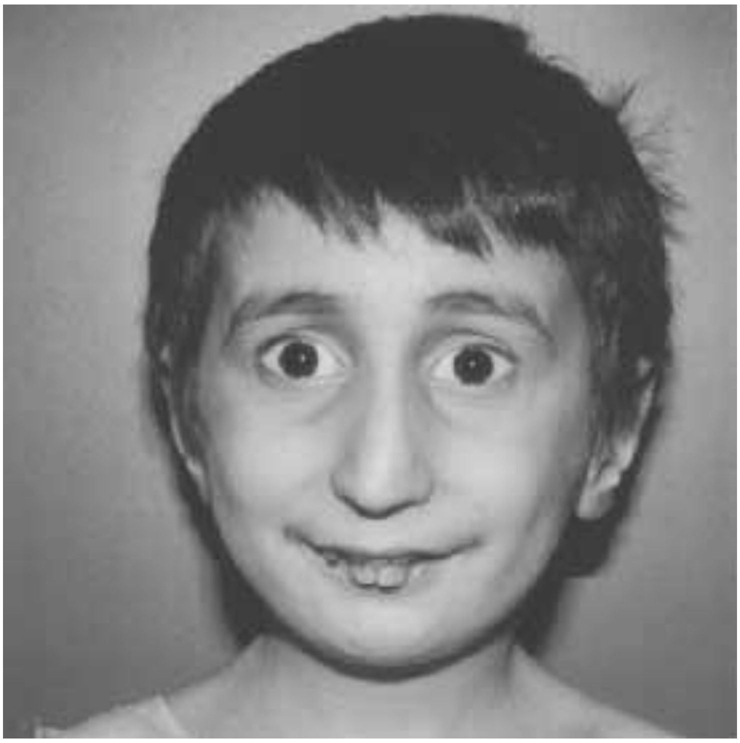


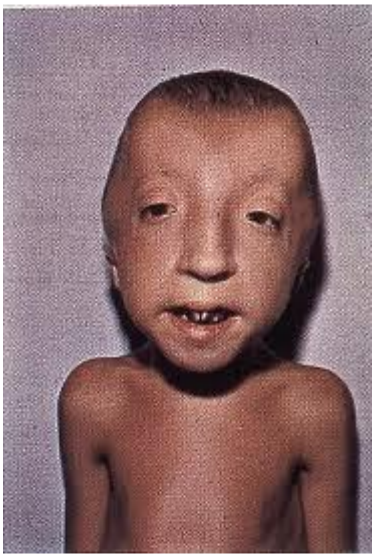


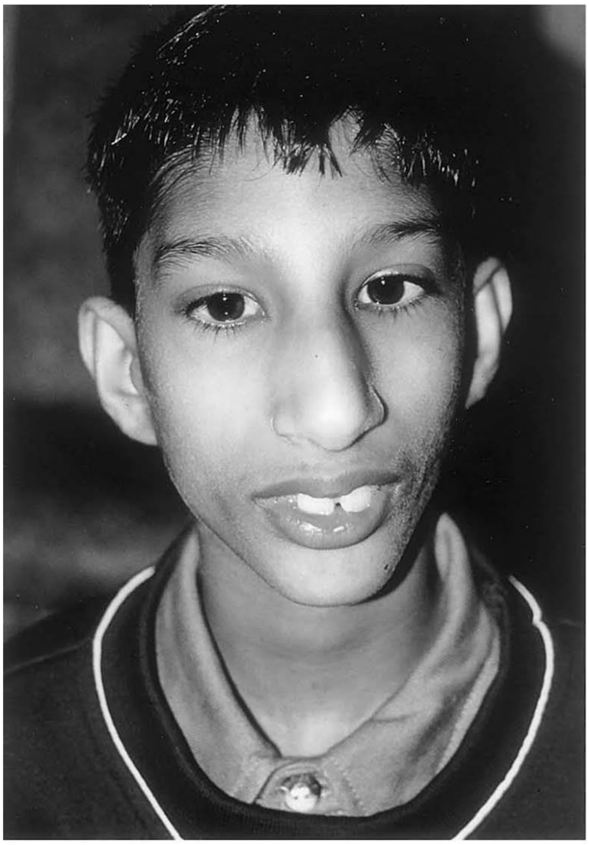


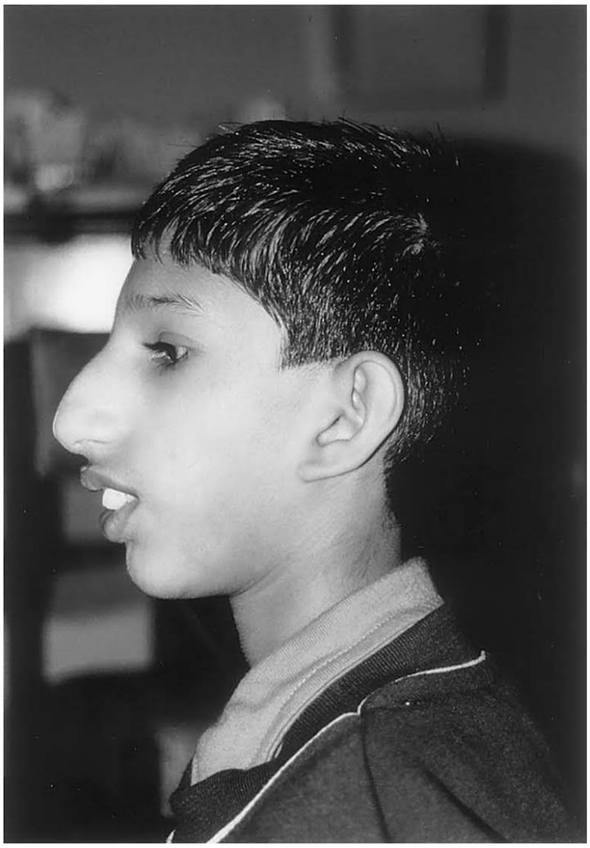
Seckel Syndrome

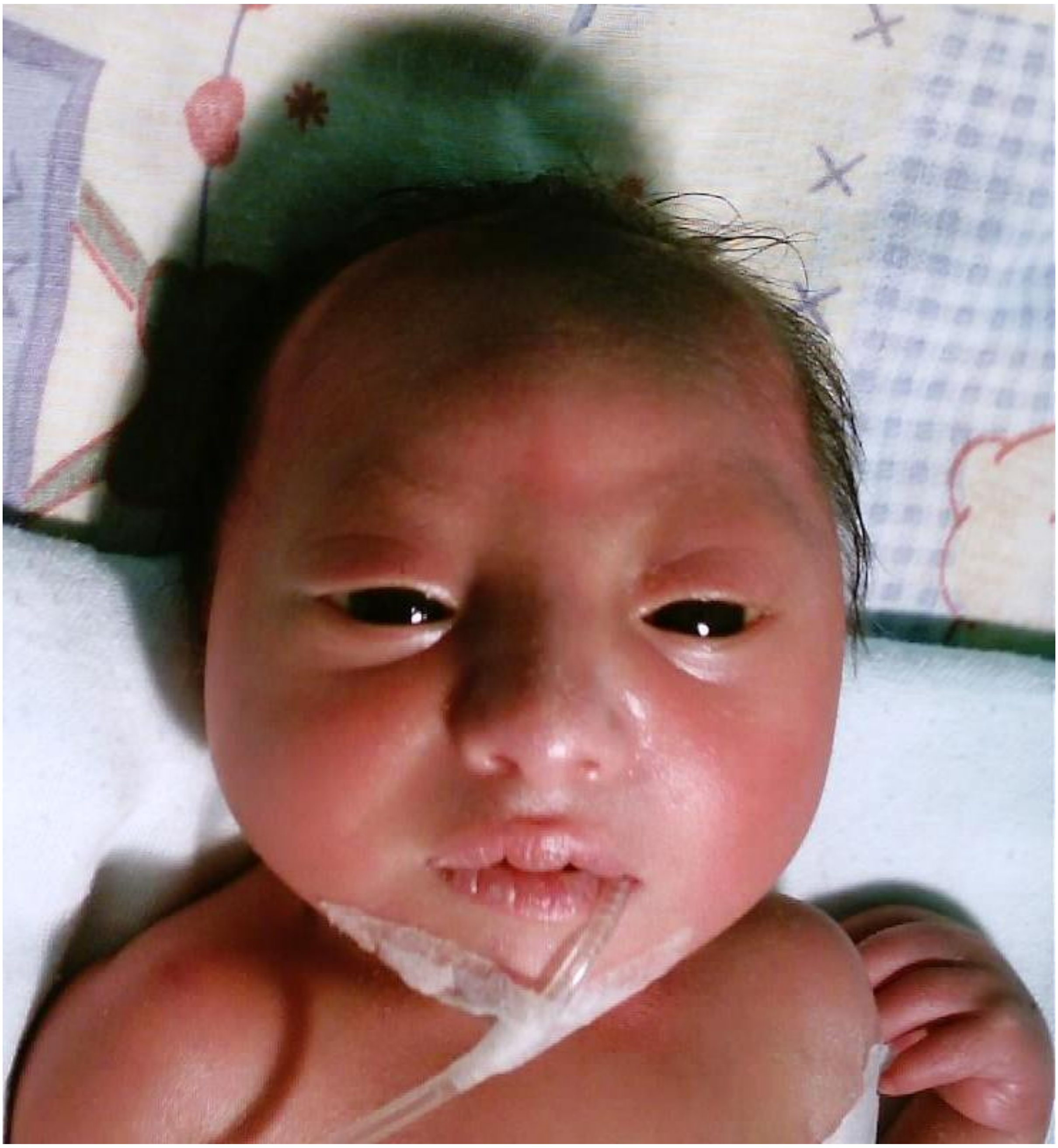
Seckel (SCKL) syndrome, sometimes called "bird-headed dwarfism," is an autosomal recessive developmental disorder characterized by marked growth failure and mental deficiency, microcephaly, a hypoplastic face with a prominent nose, and low-set and/or malformed ears. Approximately 25% of patients have aplastic anemia or malignancies.





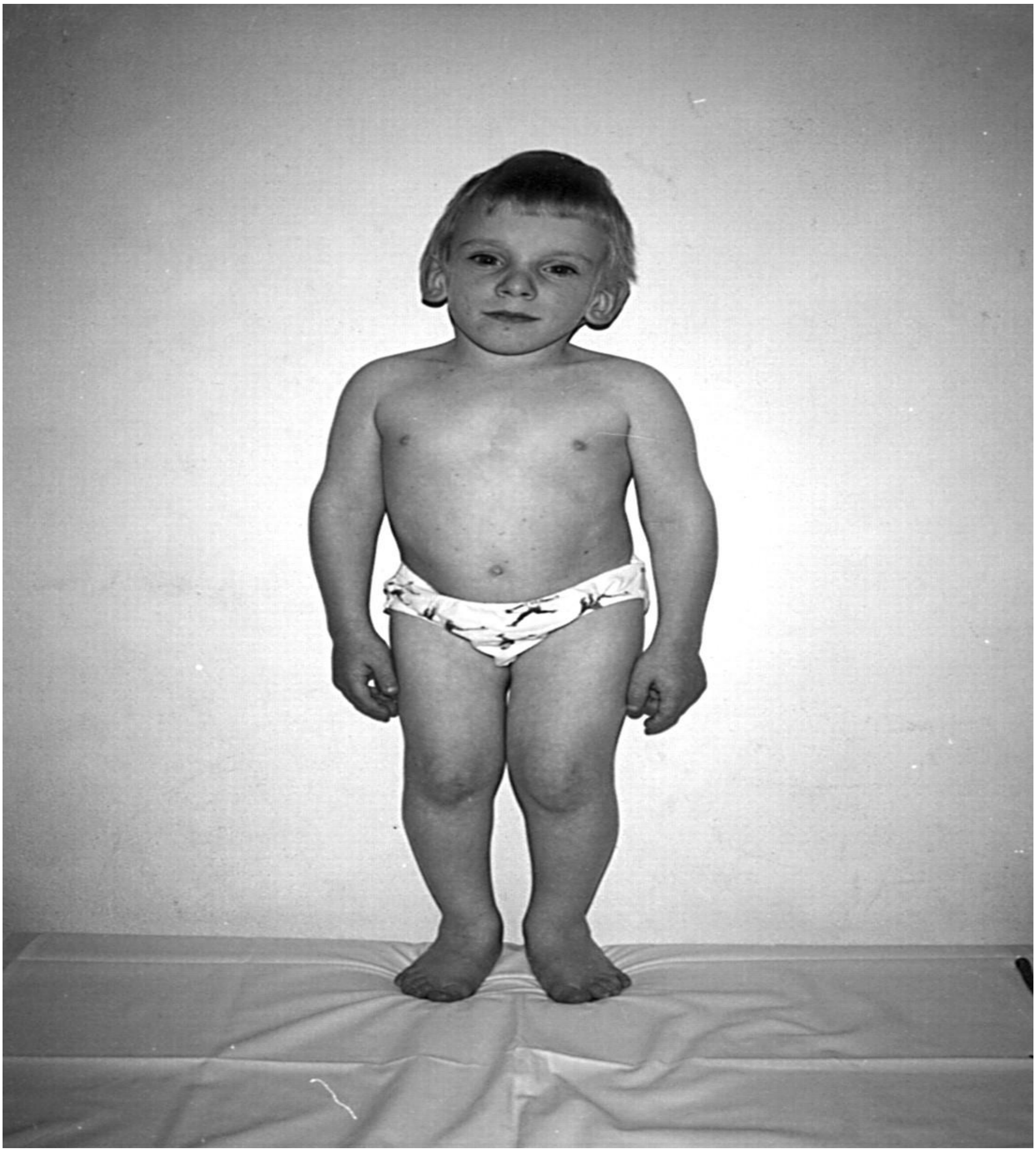






Schimke Immunoosseous Dysplasia

Schimke immunoosseous dysplasia is an autosomal recessive disorder caused by mutations in the chromatin remodeling protein *SMARCAL1*. Patients have spondyloepiphyseal dysplasia with exaggerated lumbar lordosis and a protruding abdomen. There are pigmentary skin changes and abnormally discolored and configured teeth. Renal # dysfunction can be problematic, with proteinuria and nephrotic syndrome. Approximately 50% of patients have hypothyroidism, 50% have cerebral ischemia, and 10% have bone marrow failure with neutropenia, thrombocytopenia, and anemia, and about 5% are predisposed to non- Hodgkin lymphoma. Lymphopenia and altered cellular immunity are present in almost all patients. In 2 published case reports, 2 patients underwent successful bone marrow transplantation.

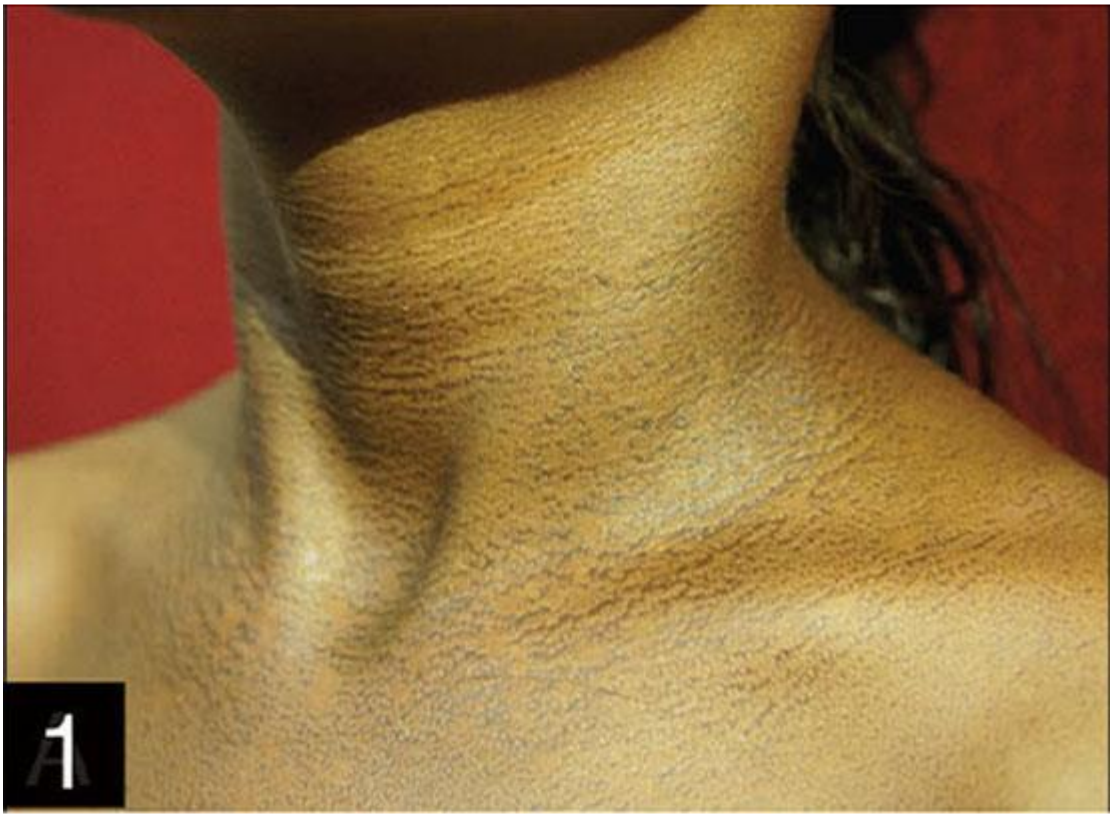


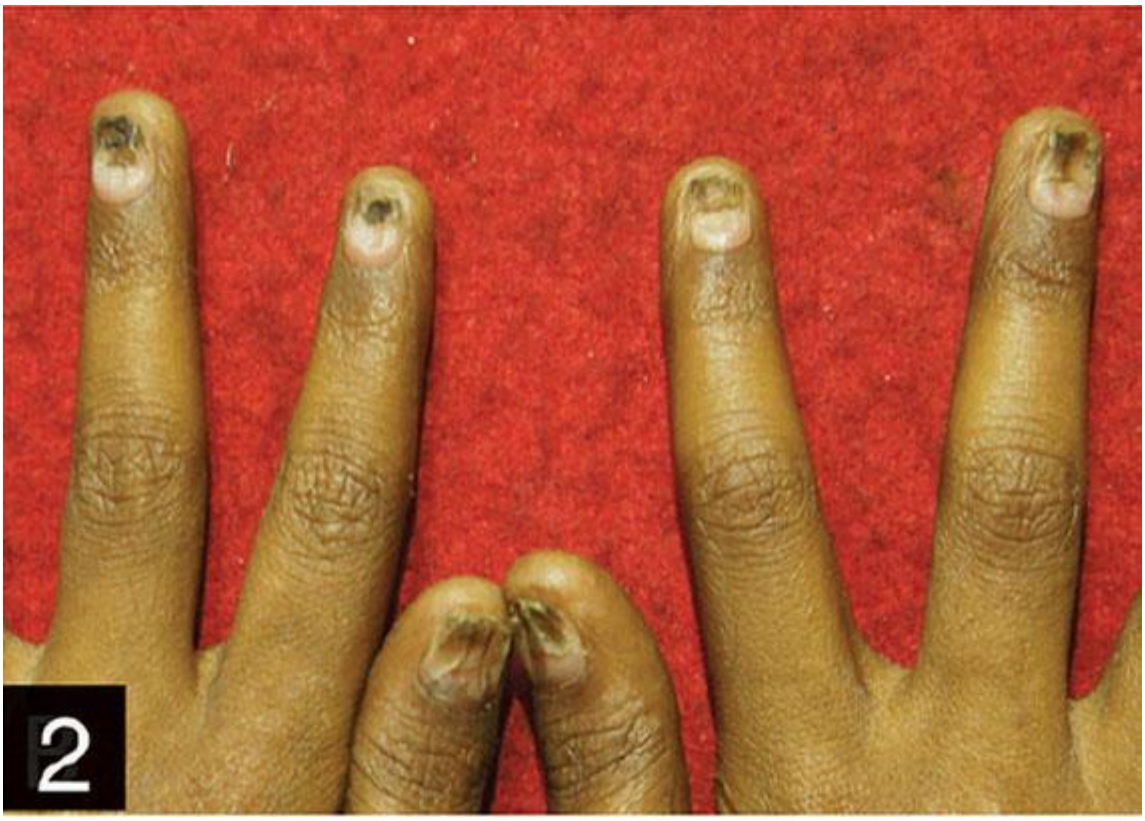
Hoyeraal-Hreidarsson syndrome

Multisystem disorder comprising aplastic anemia, immunodeficiency, microcephaly, growth retardation, and cerebellar hypoplasia.

Revesz syndrome

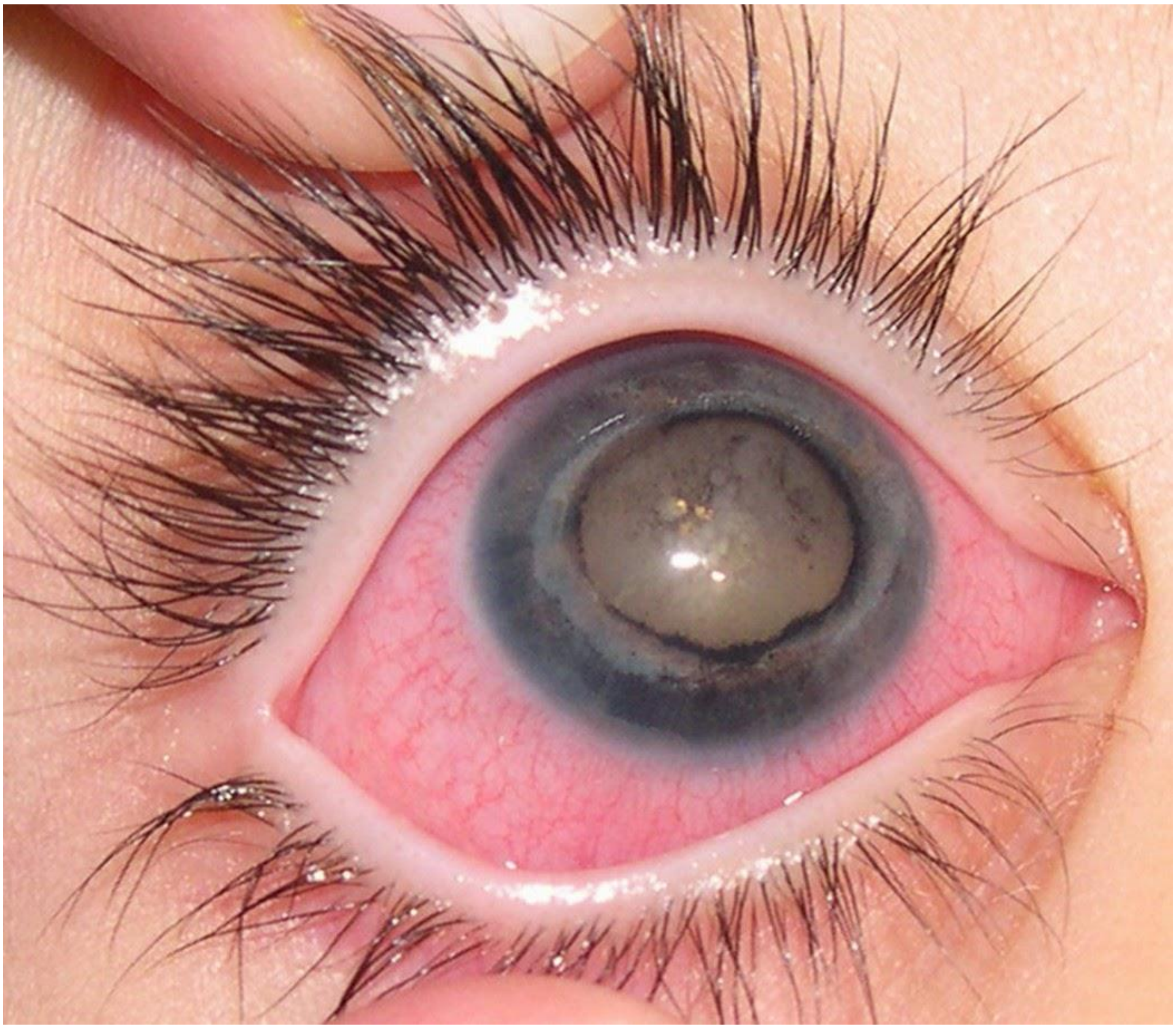
Consists of dystrophic nails, leukoplakia, aplastic anemia, cerebellar hypoplasia, growth retardation, microcephaly, and bilateral exudative retinopathy.





Coats' plus syndrome

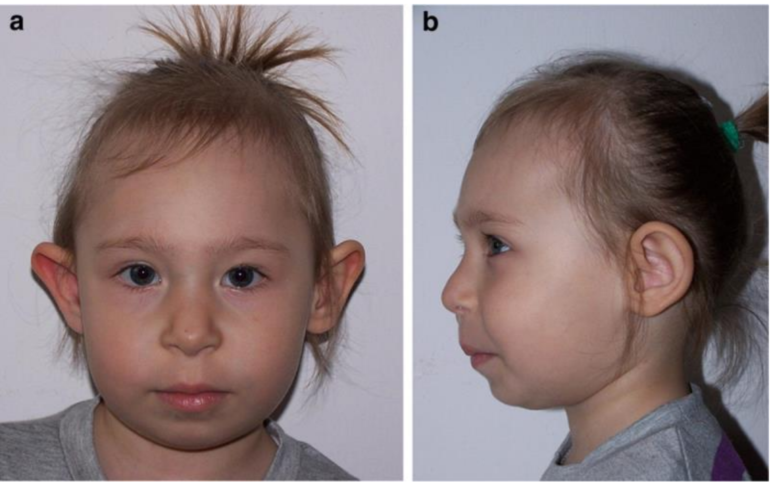
It is characterized by retinal telangiectasia and exudates, intracranial calcification, leukodystrophy, brain cysts, osteopenia, gastrointestinal bleeding and portal hypertension caused by the development of vasculature ectasias in the stomach, small intestine and liver.
Some patients with this disease has the additional manifestations of dyskeratosis congenita, which include sparse and graying hair, dystrophic nails, and anemia.

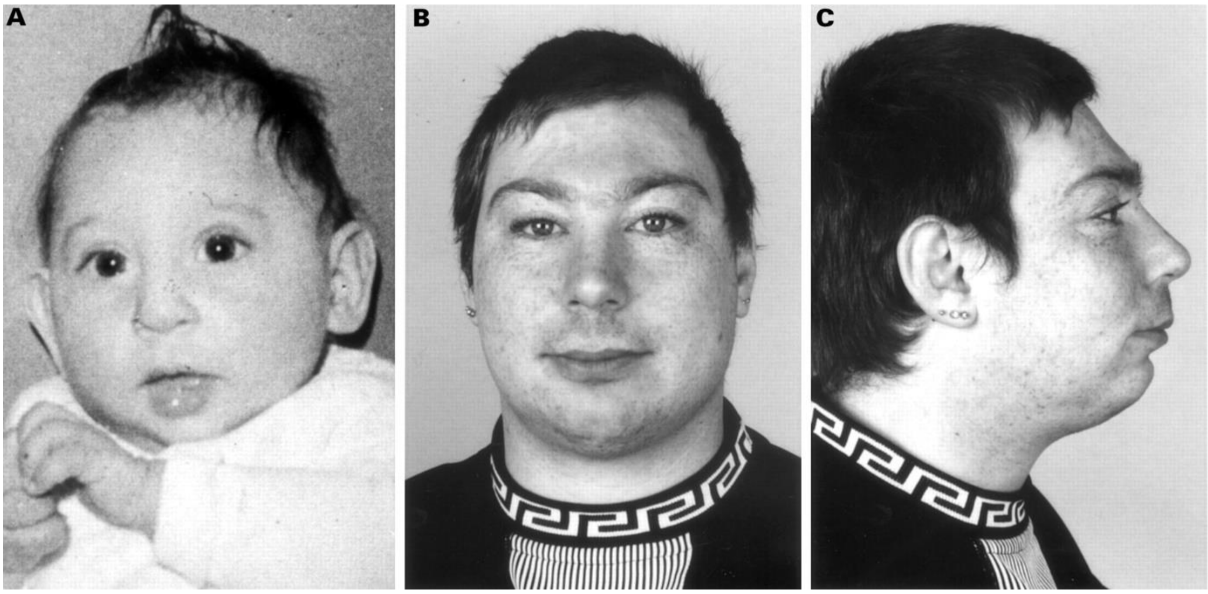


Immunodeficiency syndromes

Nijmegen breakage syndrome

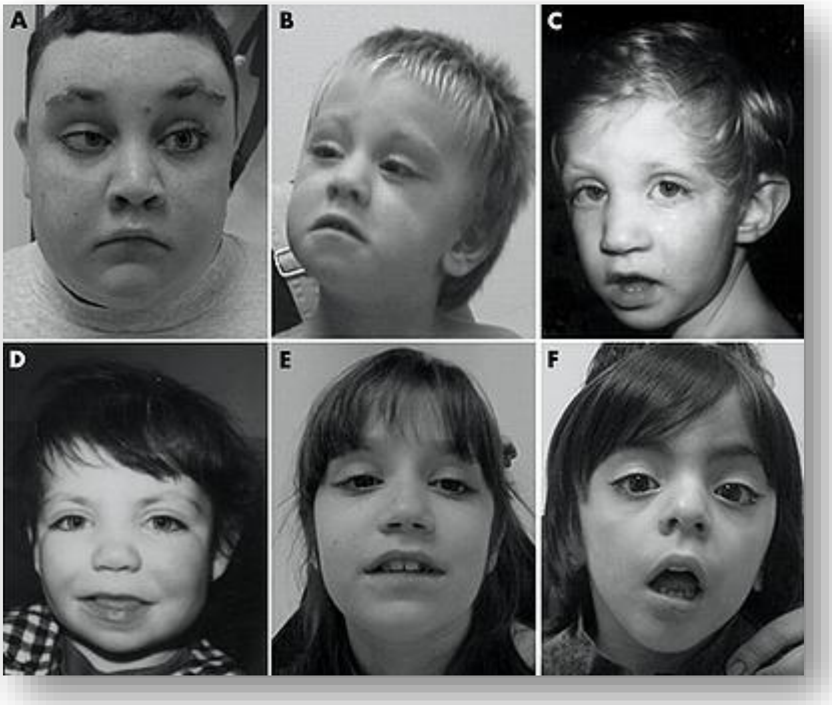
Short stature, growth retardation, microcephaly, cleft lip/palate, dysmorphic facies, bronchiectasis, sinusitis, dysgammaglobulinemia with recurrent urinary tract and gastrointestinal infections, mental retardation, spontaneous chromosomal instability, predisposition to malignancy

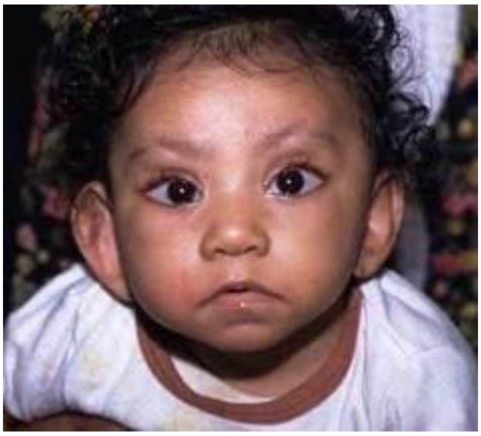


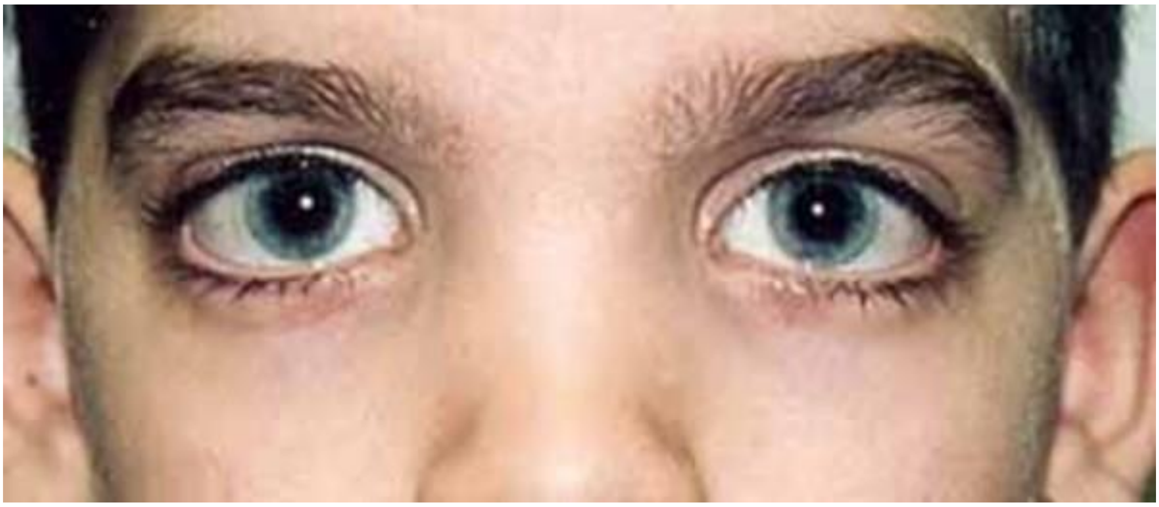


Kabuki Syndrome

Patients have long palpebral fissures with eversion of the lateral portion of the lower eyelids, prominent eyelashes, arching of the eyebrows with sparse lateral third, ptosis, large protuberant ears, and open mouth with tented upper lip. This syndrome derives its name from the resemblance of patients to the made-up actors in Japanese Kabuki theater. Immune abnormalitis include hypogammaglobulinemia (low IgG and IgA) as well as impaired specific antibody responseز







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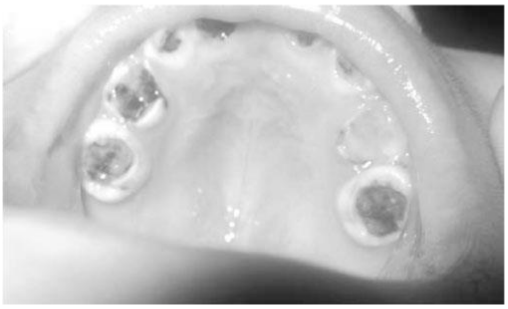
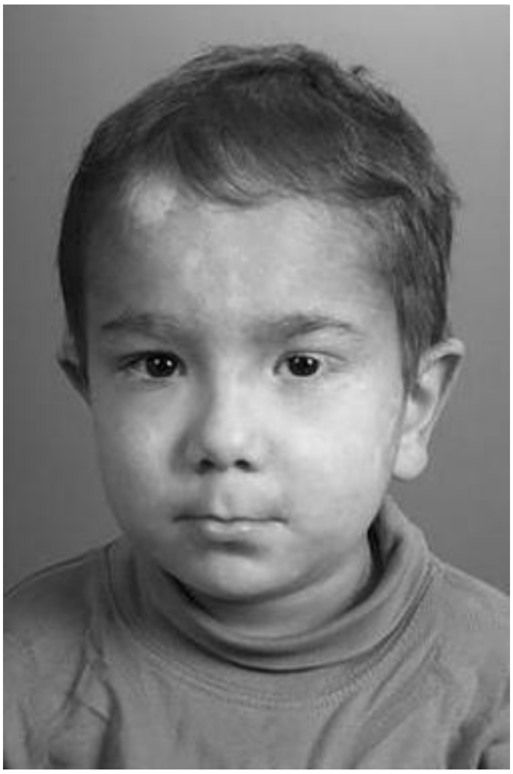
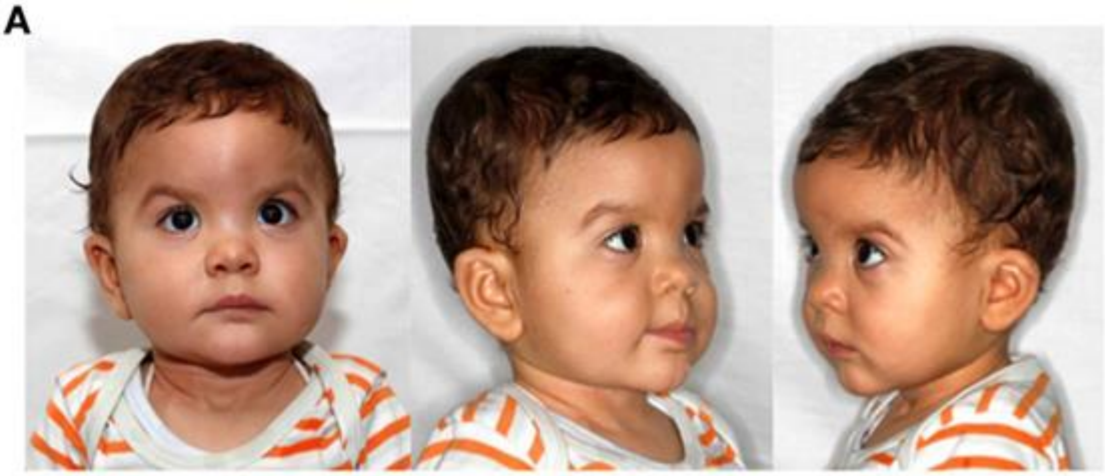


ICF Syndrome

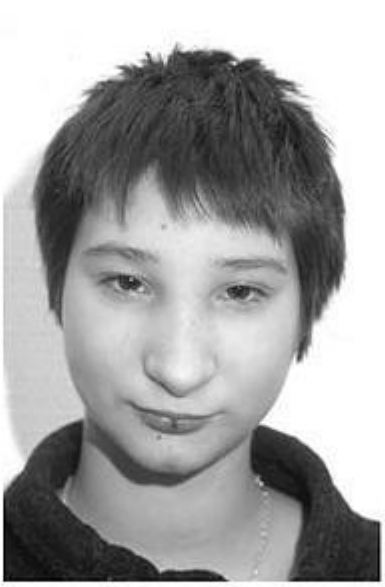
Patients are characterized by immunodeficiency (humoral and cell-mediated), centromeric instability, and facial anomalies. The facial features are characterized by hypertelorism, flat nasal bridge, epicanthal folds, and low set ears. Immune abnormalities may include decreased immunoglobulin levels as well as decreased t cell numbers and function.

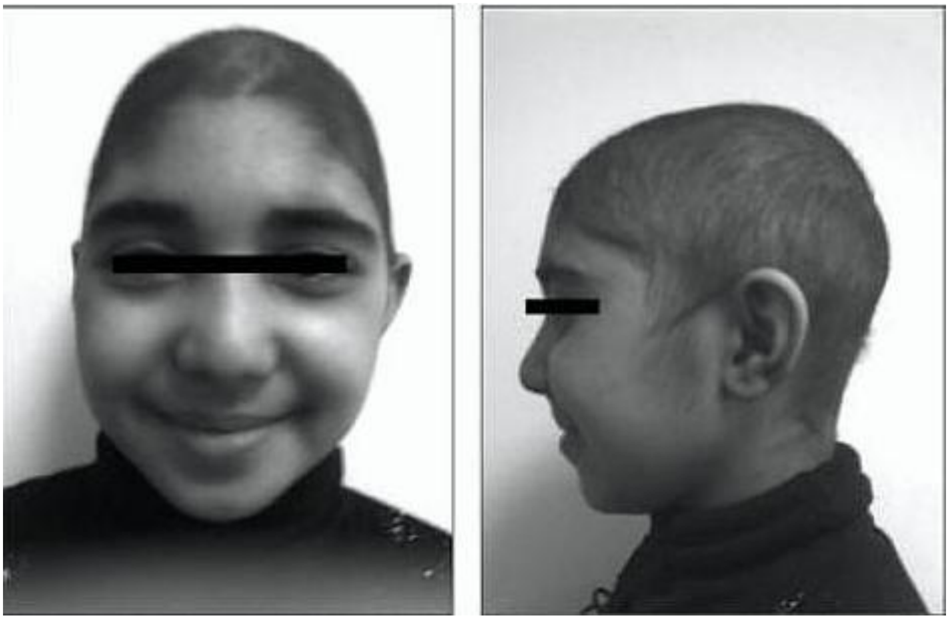


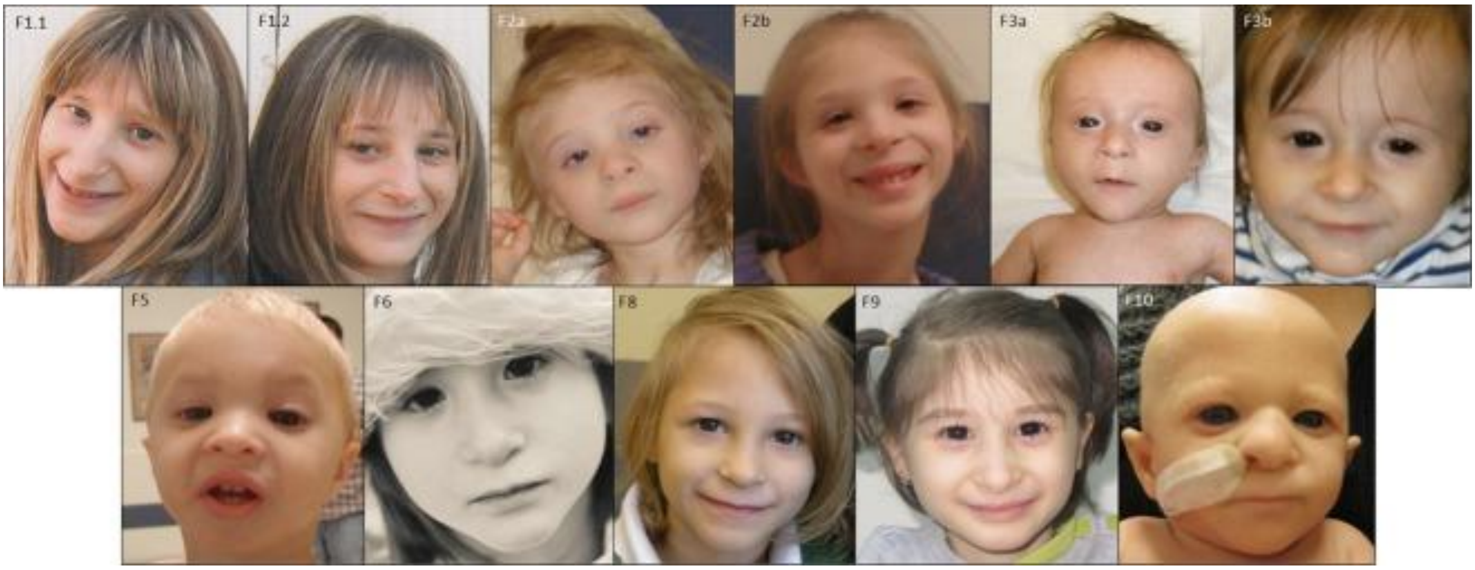


DNA Ligase IV Deficiency

Patients have microcephaly, broad nasal bridge and broad nasal tip. Patients with bird-like facies have also been reported. The immunologic phenotype can range from T-B-NK+ SCID to milder degrees of lymphopenia and hypogammaglobulinemia. Pancytopenia from marrow failure has been reported in some patients.

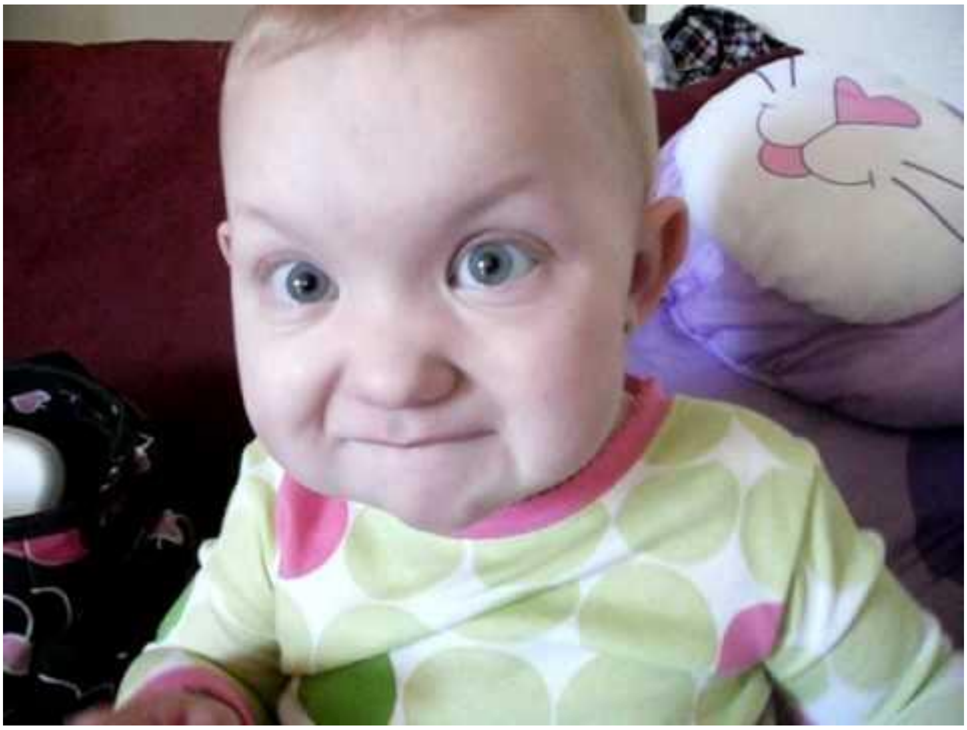


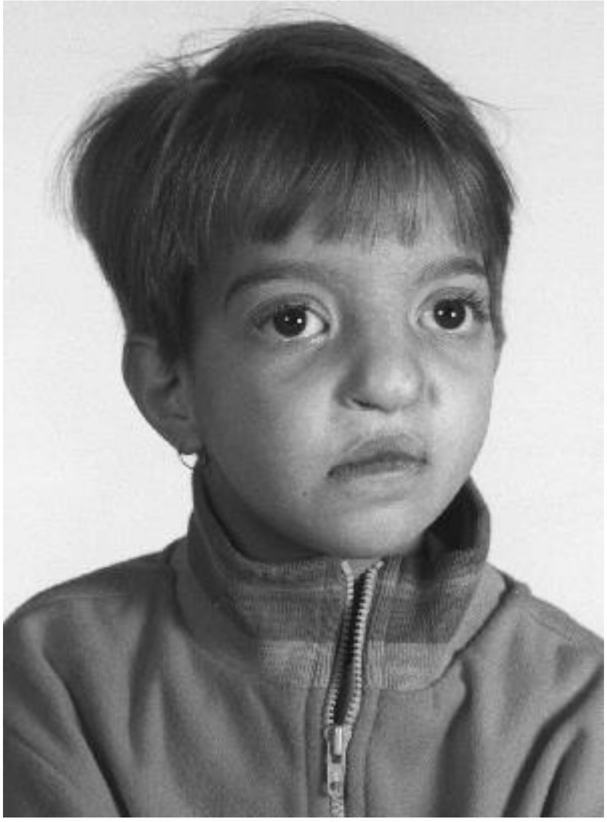


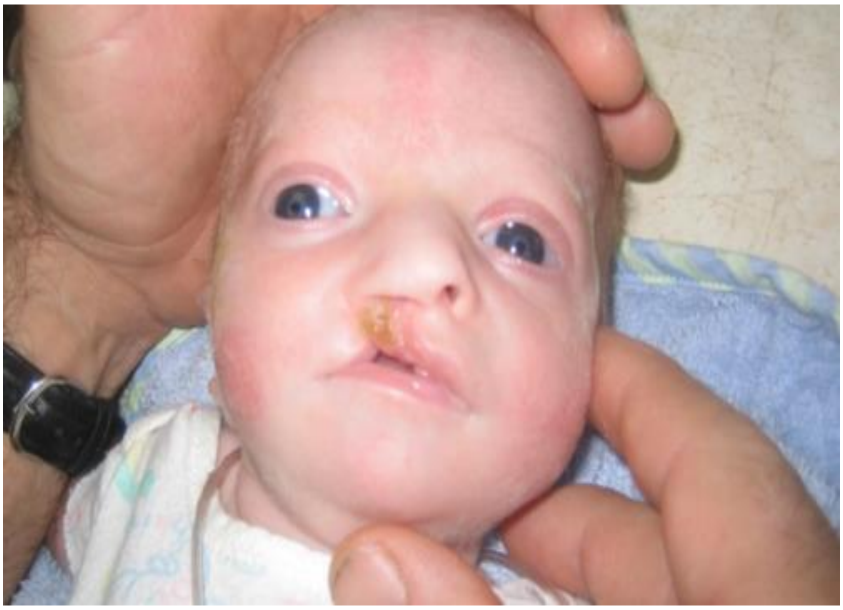


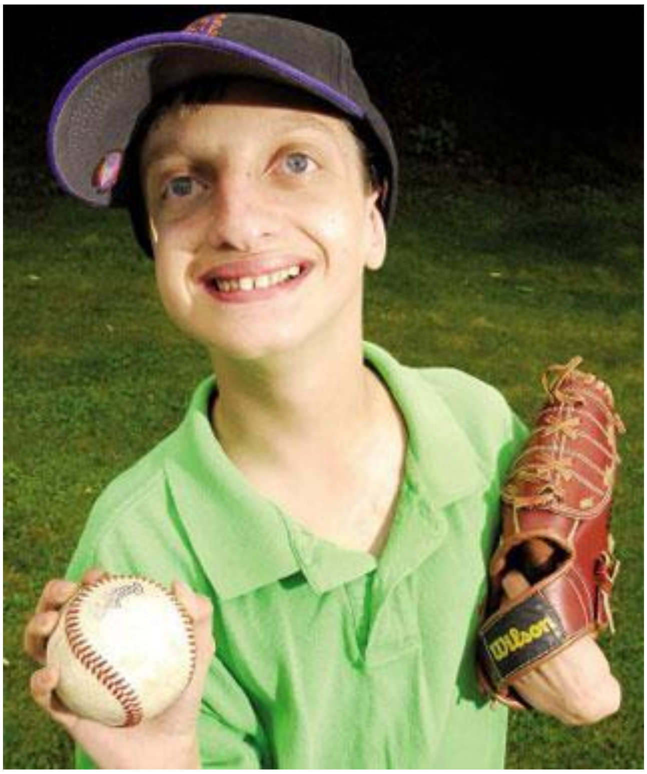
Deletion of 4p16
Wolf-Hirschhorn syndrome.

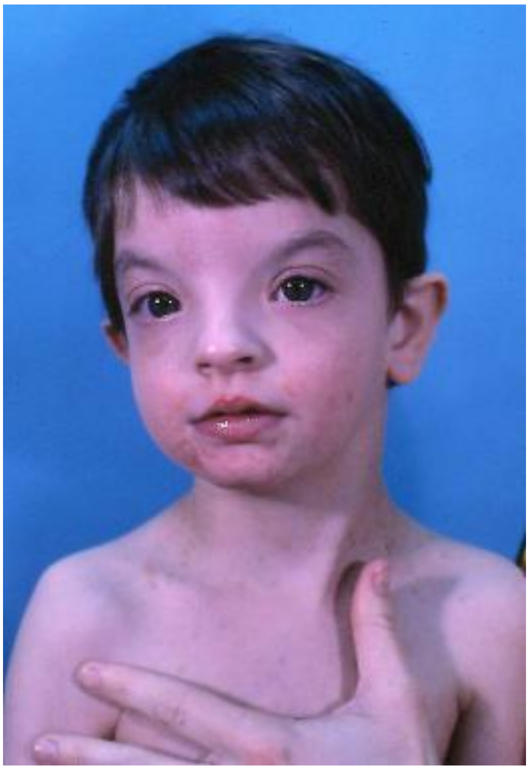
The main features are a typical "Greek helmet" facies secondary to ocular hypertelorism, prominent glabella, and frontal bossing; microcephaly, dolichocephaly, hypoplasia of the orbits, ptosis, strabismus, nystagmus, bilateral epicanthic folds, cleft lip and palate, beaked nose with prominent bridge, hypospadias, cardiac malformations, and intellectual disability.

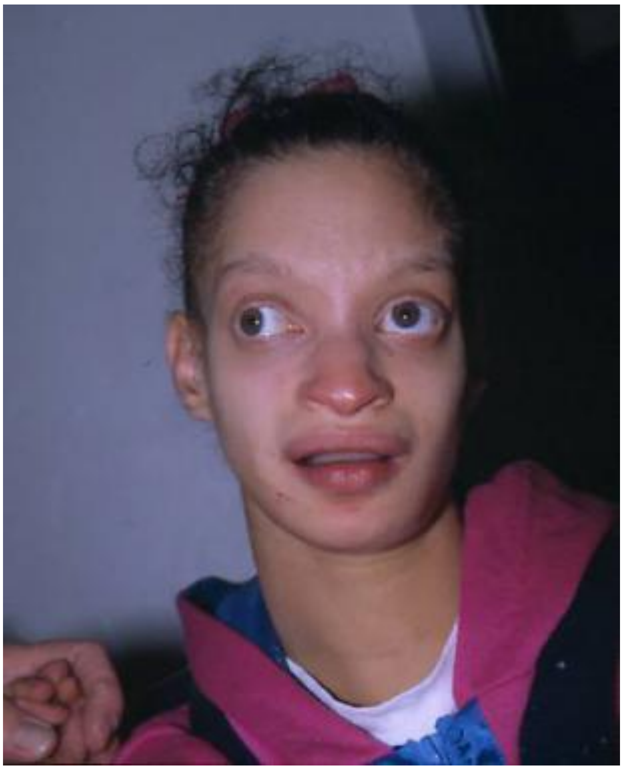






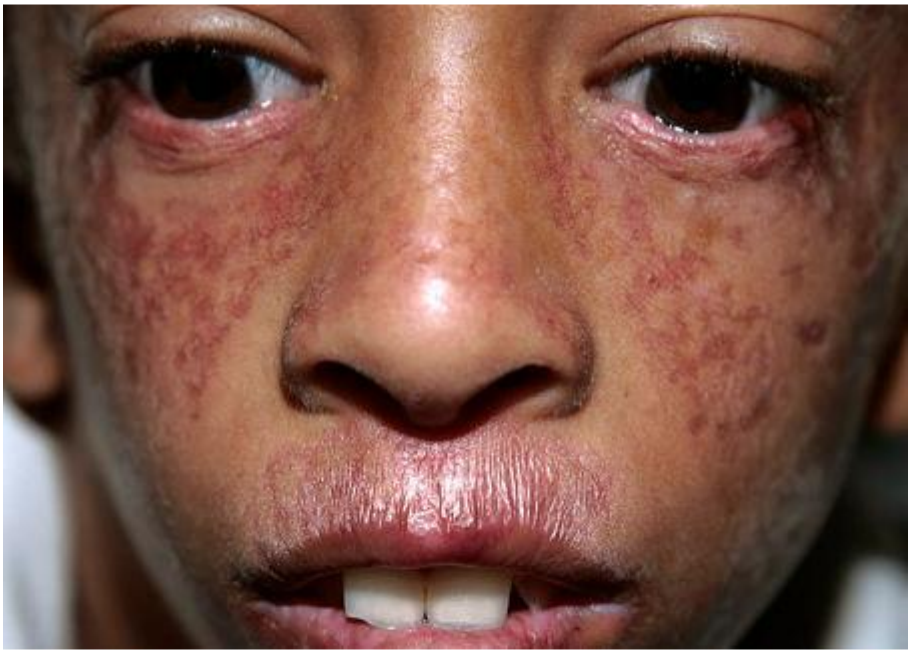


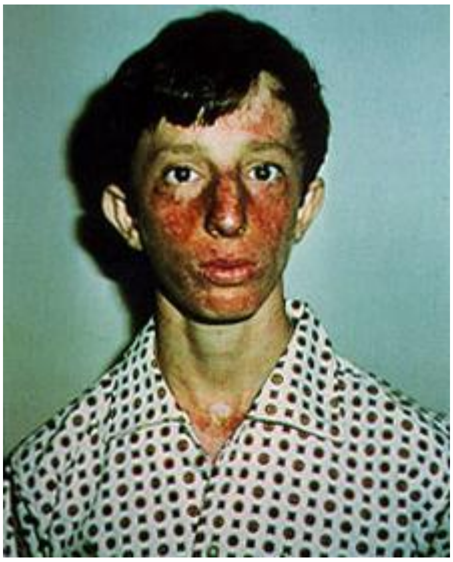


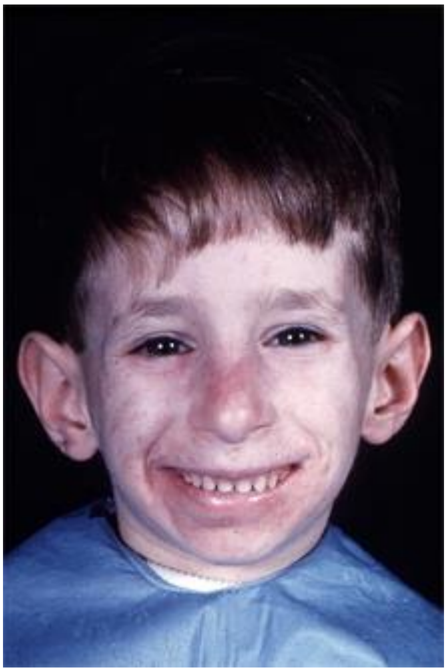


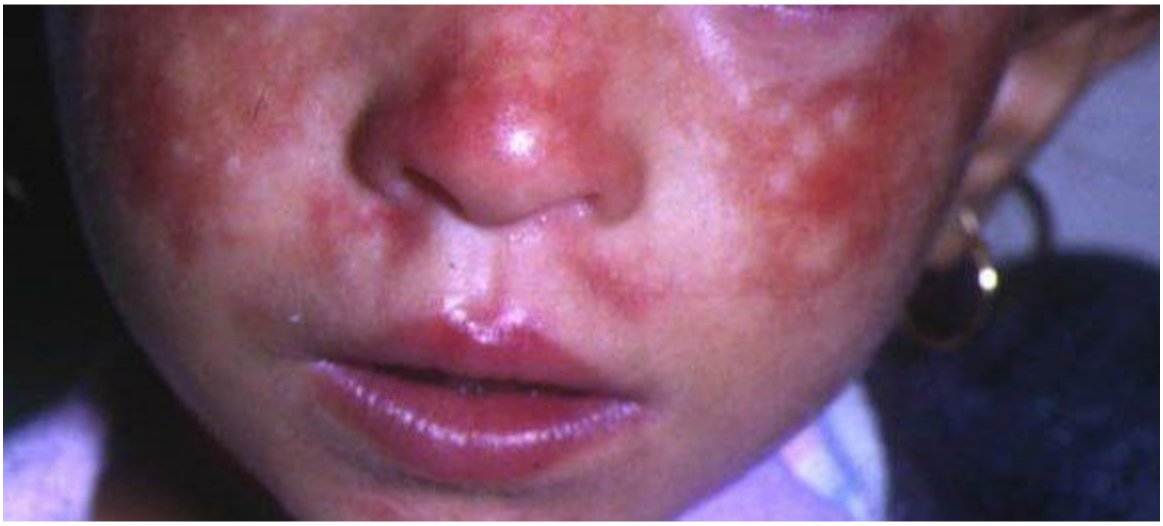
Bloom Syndrome

Erythema and telangiectasia develop during infancy in a butterfly distribution on the face after exposure to sunlight. A bullous eruption on the lips and telangiectatic erythema on the hands and forearms may develop. Café-au-lait spots and hypopigmented macules may be present. Intrauterine growth deficiency developing into short stature and a distinctive facies consisting of a prominent nose and ears and a small, narrow face are generally found. Intellect is average to low average. Immunodeficiency is seen in all patients, manifesting as recurrent ear and pulmonary infections. Gastrointestinal malabsorption, gastroesophageal reflux, and hypogonadism are common. Affected children have an unusual tendency to develop both solid tumors (especially of the skin) and lymphoreticular malignancies, which often result in death during childhood or early adulthood. Sister chromatid exchange analysis is generally performed to confirm diagnosis. The only effective measures to reduce skin disease are sun protection and avoidance.



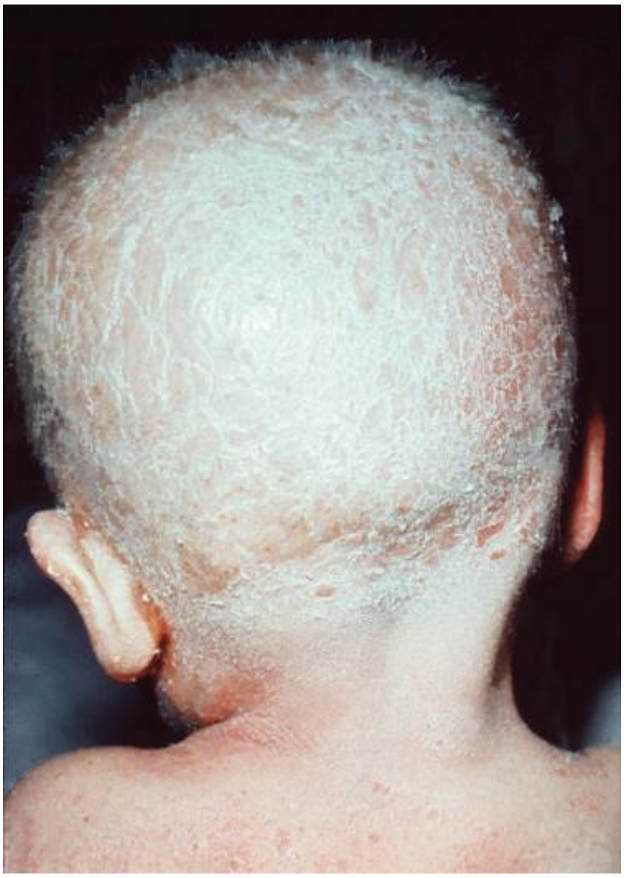


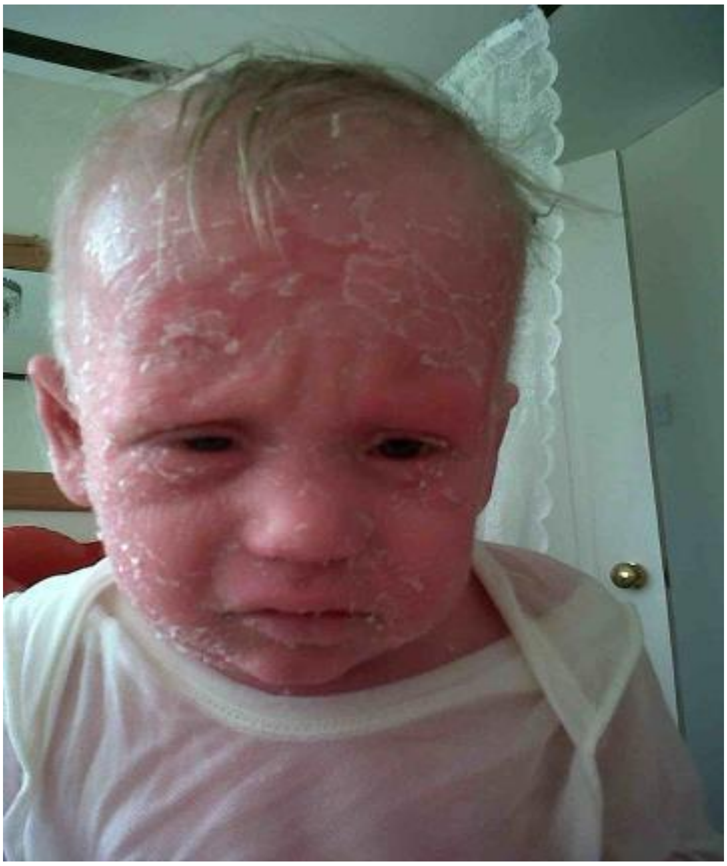


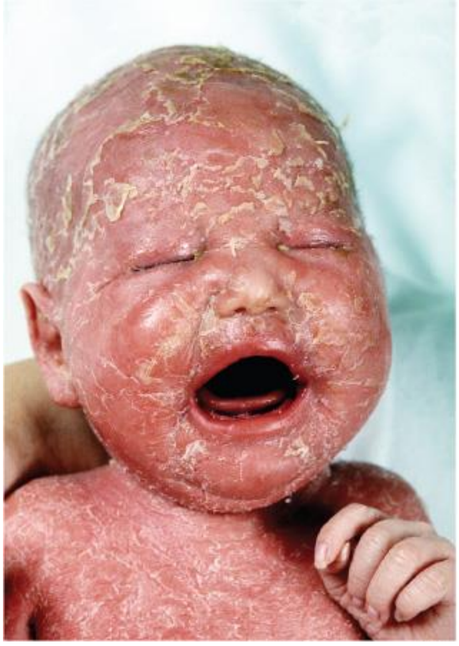


Netherton syndrome

is a type of ichthyosis. Symptoms vary but commonly include inflamed, red, scaly skin, short, brittle, lustreless hair, and a predisposition to allergy problems (e.g., to nuts, hay fever, and asthma). Symptoms may be mild or severe and tend to present in infancy. Failure to thrive and recurrent infection are possible complications in infants with this syndrome.

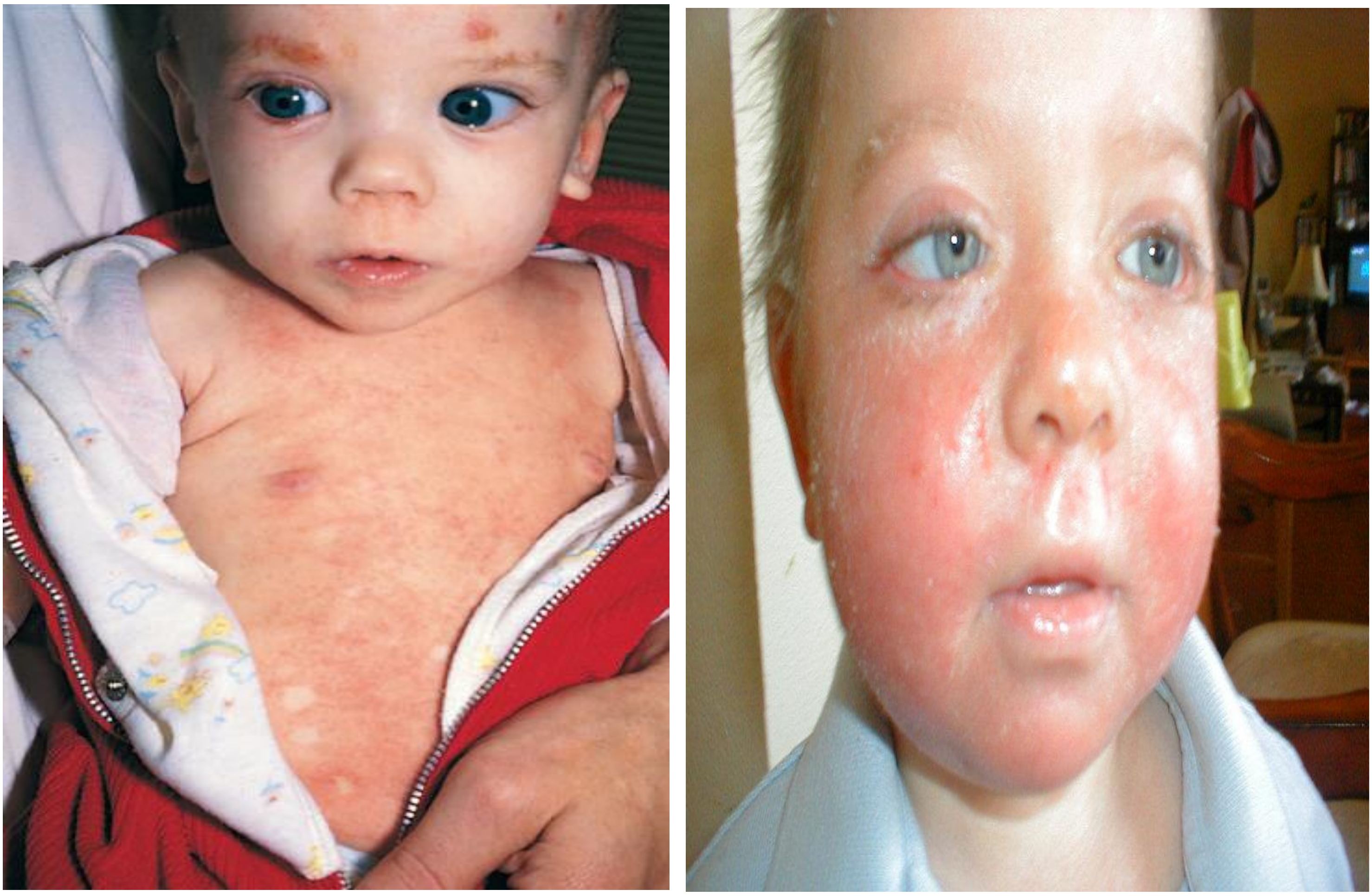


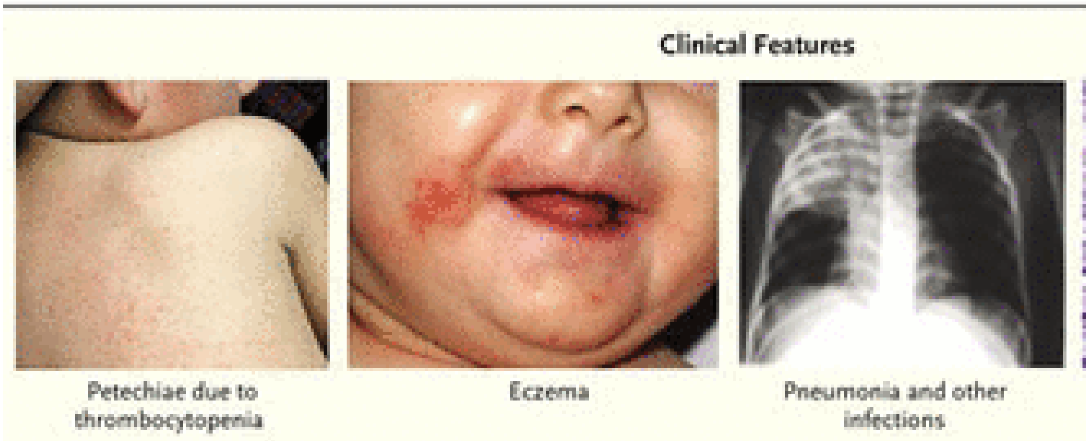




Wiskott-Aldrich syndrome

Wiskott-Aldrich syndrome, an X-linked recessive syndrome, is characterized by atopic dermatitis, thrombocytopenic purpura with normal-appearing megakaryocytes but small defective platelets, and undue susceptibility to infection.




Clinical Features

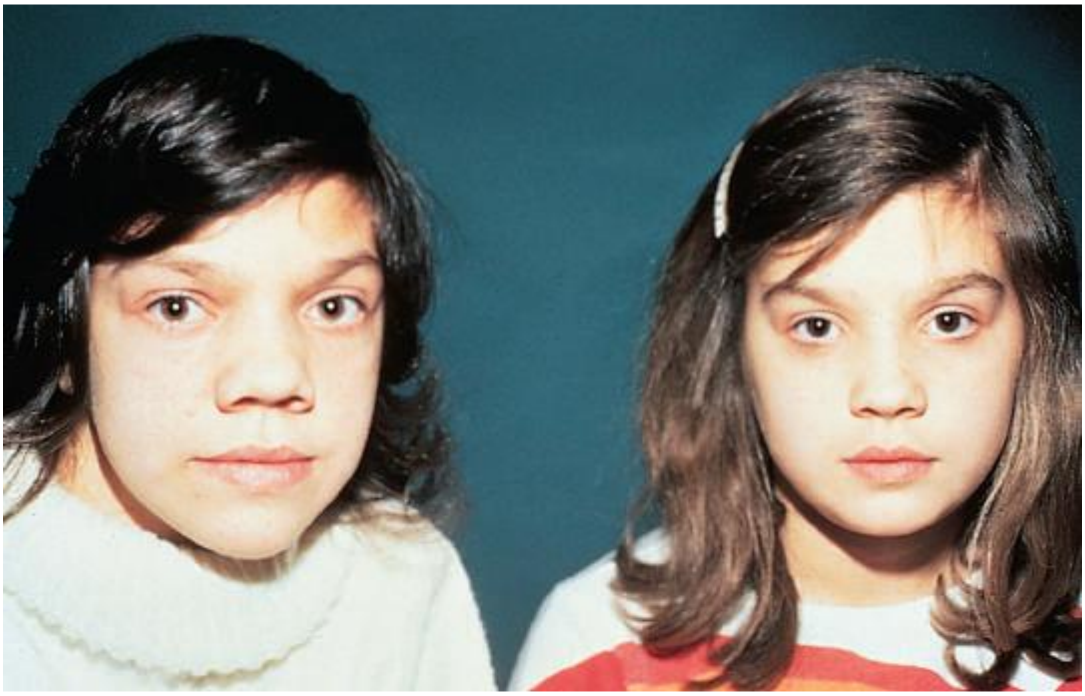
Petechiae due to thrombocytopenia

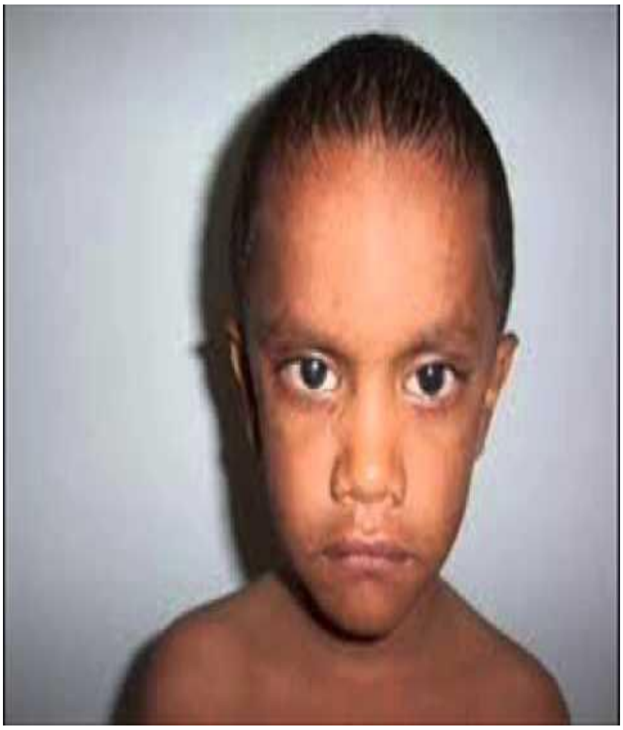
Eczema

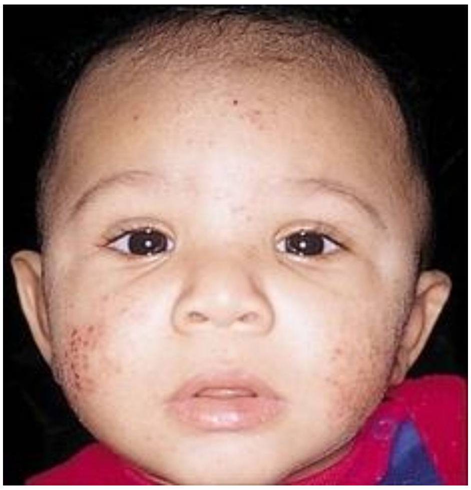
Pneumonia and other infections

Hyper-IgE Syndromes

Initially called *Job syndrome,* this disorder was characterized by the triad of eczema, recurrent skin infections, and recurrent pulmonary infections. These patients present with rash during the first weeks of life, and progress to recurrent staphylococcal skin infections, including impetigo, boils, and furuncles, which lack inflammation and are called *cold abscesses.* Staphylococcal pneumonia complicated by pneumatocele formation and lung abscesses are frequent. Candidiasis of the skin and nails is common, as well as mucocutaneous candidiasis.

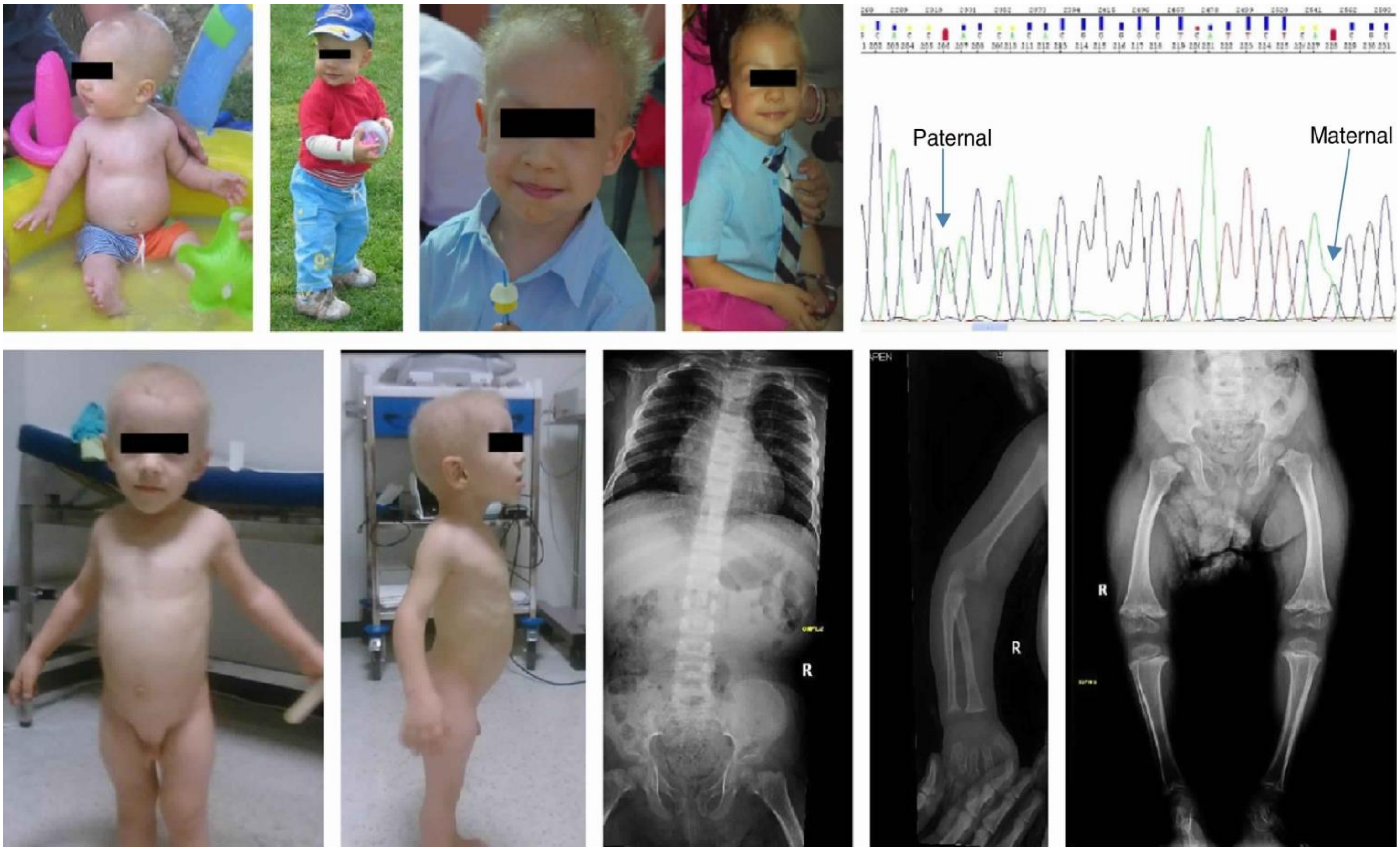






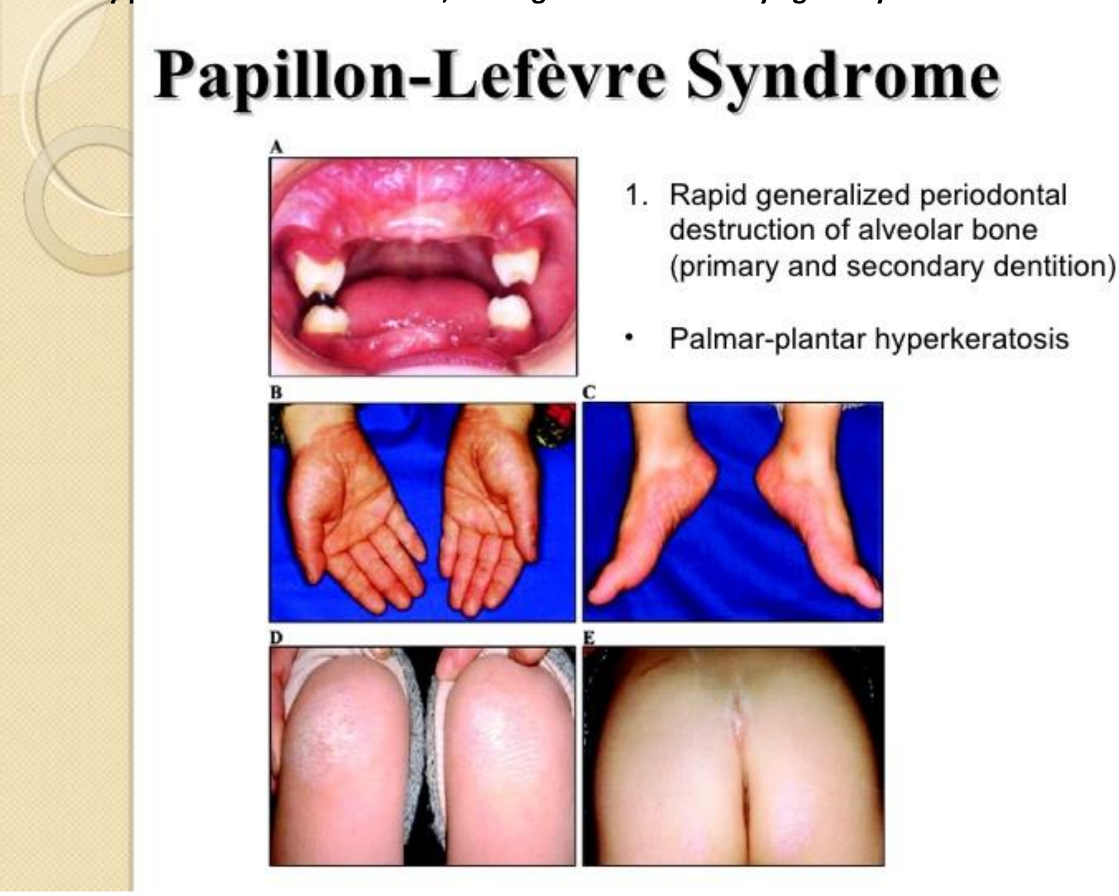
Cartilage Hair Hypoplasia

Clinical features include short, pudgy hands; redundant skin; hyperextensible joints of hands and feet but an inability to extend the elbows completely; and fine, sparse, light hair and eyebrows. Severe and often fatal varicella infections, progressive vaccinia, and vaccine-associated poliomyelitis have been observed. Associated conditions include deficient erythrogenesis, Hirschsprung disease, and an increased risk of malignancies. The bones radiographically show scalloping and sclerotic or cystic changes in the metaphyses and flaring of the costochondral junctions of the ribs. Three patterns of immune dysfunction have emerged: defective antibody-mediated immunity, CID (most common), and SCID.



Papillon-Lefèvre Syndrome

An autosomal recessive erythematous hyperkeratosis of the palms and soles, Papillon-Lefèvre syndrome sometimes extends to the dorsal hands and feet, elbows, and knees later in childhood. The palmoplantar keratoderma may be either diffuse, striate, or punctuate. This syndrome is characterized by periodontal inflammation, leading to loss of teeth by age 4-5 yr if untreated.



Papillon-Lefèvre Syndrome

1. Rapid generalized periodontal destruction of alveolar bone (primary and secondary dentition)

- Palmar-plantar hyperkeratosis

HYPOHIDROTIC ECTODERMAL DYSPLASIA

Classic presentation for features of X-linked recessive hypohidrotic ectodermal dysplasia at 1 to 20 months of age. At 1 month the infant was admitted to “rule out sepsis” with high fever, but all the workup was negative. A, Note the thin, sparse, fine hair. B, Severe hypodontia and anterior conical teeth. C, Low nasal bridge, periorbital wrinkling, full forehead, prominent lips, and prominent supraorbital ridges. Deoxyribonucleic acid (DNA) analysis of the *EDA1* gene at the Xq12 region showed the missense mutation and confirmed the clinical diagnosis. The mother and her maternal female relatives have variable and milder clinical features.